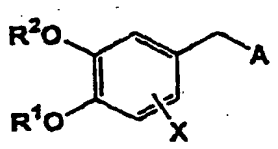
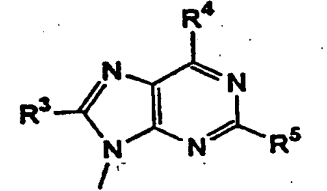
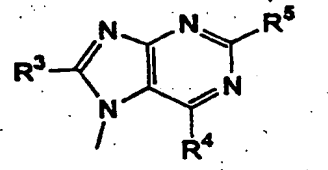
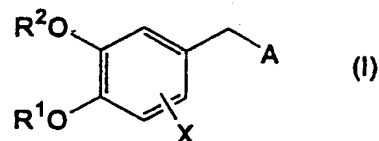




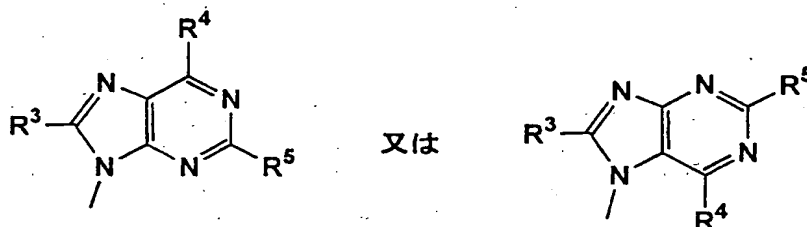
<p>(51) 国際特許分類6 C07D 473/00, 473/06, 473/16, 473/18, 473/28, 473/32, 473/34, 473/40, 239/48, 239/50, A61K 31/52, 31/535</p>	<p>A1</p>	<p>(11) 国際公開番号 WO99/24432</p> <p>(43) 国際公開日 1999年5月20日(20.05.99)</p>
<p>(21) 国際出願番号 PCT/JP98/05092</p> <p>(22) 国際出願日 1998年11月12日(12.11.98)</p> <p>(30) 優先権データ 特願平9/310365 1997年11月12日(12.11.97) JP</p> <p>(71) 出願人 (米国を除くすべての指定国について) 三菱化学株式会社 (MITSUBISHI CHEMICAL CORPORATION)[JP/JP] 〒100-0005 東京都千代田区丸の内2丁目5番2号 Tokyo, (JP)</p> <p>(72) 発明者 ; および</p> <p>(75) 発明者 / 出願人 (米国についてのみ) 田中敏彦(TANAKA, Toshihiko)[JP/JP] 岩下英一郎(IWASHITA, Eiichirou)[JP/JP] 多羅尾明子(TARAO, Akiko)[JP/JP] 雨森 晃(AMENOMORI, Akira)[JP/JP] 小野裕也(ONO, Yuya)[JP/JP] 〒227-8502 神奈川県横浜市青葉区鴨志田町1000番地 三菱化学株式会社 横浜総合研究所内 Kanagawa, (JP)</p>	<p>(74) 代理人 弁理士 今村正純, 外(IMAMURA, Masazumi et al.) 〒104-0031 東京都中央区京橋1丁目5番5号 KRFビル5階 Tokyo, (JP)</p> <p>(81) 指定国 CA, CN, GB, KR, US, 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>添付公開書類 国際調査報告書</p>	
<p>(54) Title: PURINE DERIVATIVES AND MEDICINE CONTAINING THE SAME AS THE ACTIVE INGREDIENT</p> <p>(54) 発明の名称 プリン誘導体及びそれを有効成分として含む医薬</p> <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p>(I)</p> </div> <div style="text-align: center;">  <p>(II)</p> </div> <div style="text-align: center;">  <p>(III)</p> </div> </div> <p>(57) Abstract</p> <p>Purine derivatives represented by general formula (I) or salts thereof, useful as the active ingredient of medicines such as antasthmatic, wherein R¹ represents C₁-C₄ alkyl or difluoromethyl; R² represents tetrahydrofuranyl, C₁-C₇ alkyl, etc.; X represents hydrogen, halogeno or nitro; and A represents a group represented by general formula (II) or (III), wherein R³ represents hydrogen, halogeno, etc.; and R⁴ and R⁵ represent each hydrogen, halogeno, C₁-C₄ alkyl, C₁-C₄ alkoxy, etc.</p>		

(37)要約

抗喘息薬などの医薬の有効成分として有用な下記の式：



[式中、 R^1 は $C_1 \sim C_4$ のアルキル基又はジフルオロメチル基を表し； R^2 はテトラヒドロフラン基、 $C_1 \sim C_7$ のアルキル基などを表し；Xは水素原子、ハロゲン原子、又はニトロ基を表し；Aは下記の式：



[式中、 R^3 は水素原子、ハロゲン原子などを表し； R^4 及び R^5 は水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基などを表す]で示される基を表す]で表されるプリン誘導体又はその塩。

PCTに基づいて公開される国際出願のパンフレット第一頁に掲載されたPCT加盟国を同定するために使用されるコード(参考情報)

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AZ アゼルバイジャン
BA ボスニア・ヘルツェゴビナ
BB パルバドス
BE ベルギー
BF ブルキナ・ファソ
BG ブルガリア
BJ ベナン
BR ブラジル
BY ベラルーシ
CA カナダ
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LC セントルシア

LI リヒテンシュタイン
LK スリ・ランカ
LR リベリア
LS レソト
LT リトアニア
LU ルクセンブルグ
LV ラトヴィア
MC モナコ
MD モルドヴァ
MG マダガスカル
MK マケドニア
ML マリ
MN モンゴル
MR モーリタニア
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NE ニジェール
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NZ ニュージーランド
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RO ルーマニア
RU ロシア
SD スーダン
SE スウェーデン

SG シンガポール
SI スロヴェニア
SK スロヴァキア
SL シエラ・レオネ
SN セネガル
SZ スワジランド
TD チャード
TG トーゴ
TJ タジキスタン
TM トルクメニスタン
TR トルコ
TT トリニダード・トバゴ
UA ウクライナ
UG ウガンダ
US 米国
UZ ウズベキスタン
VN ヴィエトナム
YU ユーゴスラビア
ZA 南アフリカ共和国
ZW ジンバブエ

明 細 書

プリン誘導体及びそれを有効成分として含む医薬

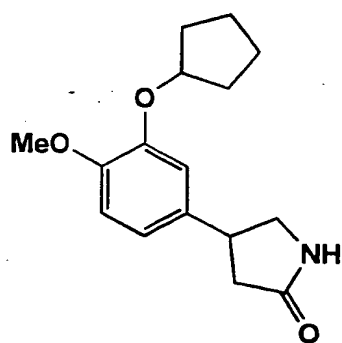
技術分野

本発明は新規なプリン誘導体に関し、より詳細にはホスホジエステラーゼ IV 阻害作用を有するプリン誘導体に関する。また、本発明は、これら新規プリン誘導体の製造用中間体にも関する。

背景技術

サイクリックAMP (cAMP) は気道平滑筋の弛緩および炎症細胞の調節に関与する重要なセカンドメッセンジャーであり、ホスホジエステラーゼ (以下、本明細書において「PDE」と略す) によって分解されて不活性な5'-AMPとなる。従って、PDEによるcAMPの分解を抑制して、cAMPの濃度を増加させることにより、気管支拡張作用および抗炎症作用が達成できると考えられる。この理由から、喘息の治療薬としてcAMPの分解を抑制する作用を有するPDE阻害薬に対する関心が高まっている。また、近年、5種類のPDEアイソザイム (PDE I、II、III、IV、V) が単離され、それらの特異的な組織分布が明らかになってきた (Adv. Second Messenger Phosphoprotein Res., 22, 1(1988); Trends Pharm., Sci., 11, 150(1990))。

これらのアイソザイムに対する阻害剤の中で、特にPDE IV に対する特異的阻害剤が喘息治療において有用である可能性が示唆されている (Thorax, 46, 512(1991))。PDE IV に特異的な阻害作用を有する化合物として、例えば、特開昭50-157360号公報に記載の化合物 (ロリブラム) が知られている。



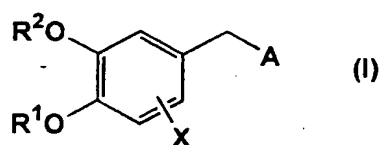
PDE IV 阻害剤としては種々の化合物が知られているが（例えば、特開平 4-253945 号公報、特表平 6-504782 号公報、特表平 7-504442 号公報、特表平 8-501318 号公報、特表平 9-500376 号公報に記載の化合物など）、現在までに臨床上適用されるには至っておらず、PDE IV 阻害作用を有する新たな化合物の開発が望まれている。

発明の開示

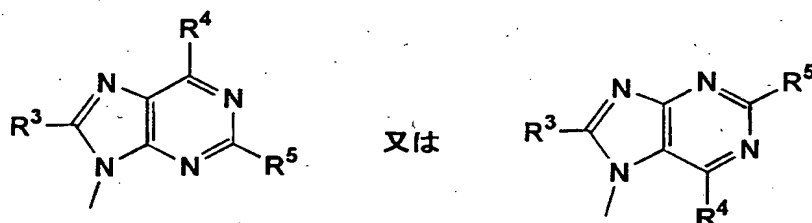
本発明の課題は、喘息治療において有用である可能性が示唆されている PDE IV に対して特異的な阻害作用を有する新規化合物を提供することにある。また、本発明の別な課題は、上記の特徴を有する化合物を有効成分として含む医薬を提供することにある。本発明のさらに別の課題は、上記の化合物を効率的に製造するための製造用中間体を提供することにある。

本発明者らは上記の課題を解決すべく鋭意研究を行った結果、下記の式で表される特定のプリン誘導体が PDE IV に対して優れた阻害作用を有していることを見出した。また、これらの化合物が医薬の有効成分として有用であり、例えば、抗喘息薬の有効成分として極めて有用であることを見出した。本発明はこれらの知見を基にして完成されたものである。

すなわち、本発明は、下記一般式 (I)：



〔式中、 R^1 は $C_1 \sim C_4$ のアルキル基又はジフルオロメチル基を表し； R^2 はテトラヒドロフラニル基、 $C_1 \sim C_7$ のアルキル基、 $C_1 \sim C_7$ のハロアルキル基、 $C_2 \sim C_7$ のアルケニル基、ビシクロ〔2，2，1〕ヘプト-2-イル基、又は $C_3 \sim C_8$ のシクロアルキル基を表し；Xは水素原子、ハロゲン原子、又はニトロ基を表し；Aは下記の式：



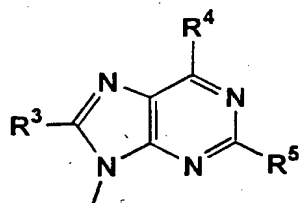
〔式中、 R^3 は水素原子、ハロゲン原子、水酸基、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基を表し； R^4 及び R^5 は、それぞれ独立に、水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、ピロリジニル基、モルホリノ基、 $C_2 \sim C_8$ のジアルキルアミノ基、又は $-Y-(CH_2)_n-B$ 〔Yは $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-N(R^6)-$ （ R^6 は水素原子又は $C_1 \sim C_4$ のアルキル基を表す）を表し、 n は0～4の整数を表し、Bはそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基を表す〕で示される基を表すが、

ただし、Xが水素原子を表す場合、 R^4 又は R^5 のいずれかは $-Y-(CH_2)_n-B$ 〔Yは $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-N(R^6)-$ （ R^6 は水素原子又は $C_1 \sim C_4$ のアルキル基を表す）を表し、

(i) Yが $-O-$ 、 $-S-$ 、又は $-NHCO-$ を表す場合には、nは0～4の整数を表し、Bはそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基を表し、

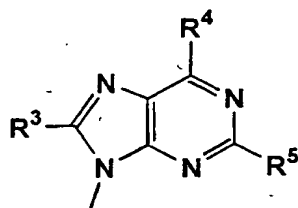
(ii) Yが $-N(R^6)-$ を表す場合には、nは1～4の整数を表し、Bは複素環残基を表す]で示される基を表す]で表されるプリン誘導体、その塩、若しくはそのN-オキシド体、又はそれらの水和物若しくはそれらの溶媒和物を提供するものである。

上記発明の好ましい態様によれば、Aが下記の式：



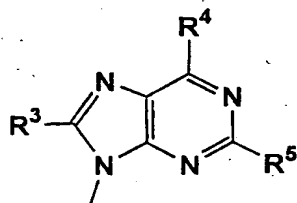
[R^3 が水素原子、ハロゲン原子、水酸基、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基であり； R^4 及び R^5 の一方が水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、ピロリジニル基、モルホリノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基であり、他方が $-Y-(CH_2)_n-B$ （Yは $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-N(R^6)-$ （ R^6 は水素原子又は $C_1 \sim C_4$ のアルキル基を表す）であり、nが0～4の整数であり、Bがそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基である]で示される基である上記プリン誘導体、その塩、若しくはそのN-オキシド体、又はそれらの水和物若しくはそれらの溶媒和物；

R^1 が $C_1 \sim C_4$ のアルキル基であり、 R^2 がテトラヒドロフラニル基、 $C_1 \sim C_6$ のアルキル基、 $C_1 \sim C_3$ のハロアルキル基、又は $C_3 \sim C_8$ のシクロアルキル基であり、Aが下記の式：



{ R^3 が水素原子、ハロゲン原子、水酸基、 $C_1 \sim C_4$ のアルキル基、又は $C_1 \sim C_4$ のアルコキシ基であり； R^4 が水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基であり、 R^5 が $-Y-(CH_2)_n-B$ (Y は $-O-$ 、 $-S-$ 、又は $-NHCO-$ であり、 n が1～4の整数であり、 B が置換基を有していてもよい複素環残基を表す) で表される基である} で表される基である上記のプリン誘導体、その塩、若しくはそのN-オキシド体、又はそれらの水和物若しくはそれらの溶媒和物；

R^1 が $C_1 \sim C_3$ のアルキル基であり、 R^2 が $C_3 \sim C_8$ のシクロアルキル基であり、 A が下記の式：



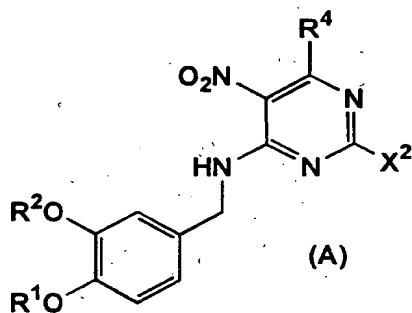
{ R^3 が水素原子、 $C_1 \sim C_3$ のアルキル基、又は $C_1 \sim C_3$ のアルコキシ基であり； R^4 が $C_1 \sim C_3$ のアルキル基、 $C_1 \sim C_3$ のアルコキシ基、 $C_1 \sim C_3$ のアルキルアミノ基であり； R^5 が $-Y-(CH_2)_n-B$ (Y が $-O-$ であり、 n が1～4の整数を表し、 B が置換基を有していてもよい複素環残基である) で表される基である} で表される基である上記のプリン誘導体、その塩、若しくはそのN-オキシド体、又はそれらの水和物若しくはそれらの溶媒和物が提供される。

別の観点からは、本発明により、上記のプリン誘導体、その塩、及びそのN-

オキシド体、並びにそれらの水和物及びそれらの溶媒和物からなる群から選ばれる物質を有効成分として含む医薬が提供される。この医薬は、好ましくは上記有効成分と製剤用添加物とを含む医薬組成物として提供され、例えば、喘息の予防及び／又は治療のための抗喘息薬として用いることができる。

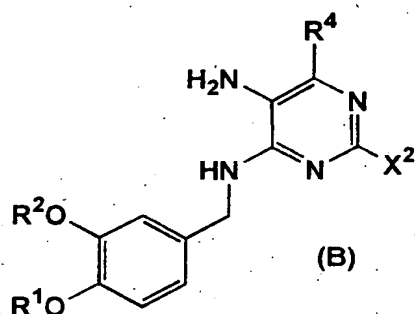
さらに別の観点からは、上記医薬の製造のための上記のプリン誘導体、その塩、及びそのN-オキシド体、並びにそれらの水和物及びそれらの溶媒和物からなる群から選ばれる物質の使用；喘息の治療及び／又は予防方法であって、上記のプリン誘導体、その塩、及びそのN-オキシド体、並びにそれらの水和物及びそれらの溶媒和物からなる群から選ばれる物質の有効量をヒトを含む哺乳類動物に投与する工程を含む方法；及び、上記のプリン誘導体、その塩、及びそのN-オキシド体、並びにそれらの水和物及びそれらの溶媒和物からなる群から選ばれる物質を含むホスホジエステラーゼ IV 阻害剤が提供される。

また、さらに別の観点からは、本発明により、下記の一般式 (A)：



〔式中、 R^1 は $C_1 \sim C_4$ のアルキル基又はジフルオロメチル基を表し； R^2 はテトラヒドロフラニル基、 $C_1 \sim C_7$ のアルキル基、 $C_1 \sim C_7$ のハロアルキル基、 $C_2 \sim C_7$ のアルケニル基、ビシクロ〔2, 2, 1〕ヘプト-2-イル基、又は $C_3 \sim C_8$ のシクロアルキル基を表し； R^4 は水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、ピロリジニル基、モルホリノ基、 $C_2 \sim C_8$ のジアルキルアミノ基、又は $Y-(CH_2)_n-B$ { Y は $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-NR^6-$ (R

⁶は水素原子又はC₁～C₄のアルキル基を表す)を表し、nは0～4の整数を表し、Bはそれぞれが置換基を有していてもよいフェニル基、ナフチル基又は複素環残基を表す)を表し、X²はハロゲン原子を表す]で示される化合物;及び下記の一般式(B):



[式中、R¹はC₁～C₄のアルキル基又はジフルオロメチル基を表し; R²はテトラヒドロフラニル基、C₁～C₇のアルキル基、C₁～C₇のハロアルキル基、C₂～C₇のアルケニル基、ビシクロ[2, 2, 1]ヘプト-2-イル基、又はC₃～C₈のシクロアルキル基を表し; R⁴は水素原子、ハロゲン原子、C₁～C₄のアルキル基、C₁～C₄のアルコキシ基、アミノ基、C₁～C₄のアルキルアミノ基、ピロリジニル基、モルホリノ基、C₂～C₈のジアルキルアミノ基、又は-Y-(CH₂)_n-B {Yは-O-, -S-, -NHCO-, 又は-N(R⁶)- (R⁶は水素原子又はC₁～C₄のアルキル基を表す)を表し、nは0～4の整数を表し、Bはそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基を表す)を表し、X²はハロゲン原子を表す]で示される化合物が提供される。これらの化合物は、上記の式(I)で表される化合物を製造するための製造用中間体として有用である。

一般式(A)又は(B)で表されるこれら製造用中間体の好ましい態様によれば、R¹がC₁～C₄のアルキル基であり、R²がテトラヒドロフラニル基、C₁～C₈のアルキル基、C₁～C₃のハロアルキル基、C₃～C₈のシクロアルキル基であり、R⁴は水素原子、ハロゲン原子、C₁～C₄のアルキル基、C₁～C₄のアル

コキシ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基である化合物が提供される。

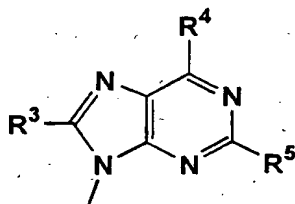
発明を実施するための最良の形態

R^1 は $C_1 \sim C_4$ の直鎖若しくは分岐鎖のアルキル基（メチル基、エチル基、 n -プロピル基、イソプロピル基、 n -ブチル基、イソブチル基、sec-ブチル基、 t -ブチル基等）、又はジフルオロメチル基を表し、好ましくは $C_1 \sim C_4$ のアルキル基、さらに好ましくは $C_1 \sim C_3$ のアルキル基、さらに好ましくはメチル基又はエチル基、特に好ましくはメチル基を表す。

R^2 はテトラヒドロフラニル基、 $C_1 \sim C_7$ の直鎖若しくは分岐鎖のアルキル基（メチル基、エチル基、 n -プロピル基、イソプロピル基、 n -ブチル基、イソブチル基、sec-ブチル基、 t -ブチル基、 n -ペンチル基、1,2-ジメチルプロピル基、1,1-ジメチルプロピル基、 n -ヘキシル基、1-メチルペンチル基、2-メチルペンチル基、3-メチルペンチル基、4-メチルペンチル基、1,1-ジメチルブチル基、2,2-ジメチルブチル基、3,3-ジメチルブチル基、1,2-ジメチルブチル基、1,3-ジメチルブチル基、1,2,2-トリメチルプロピル基、ヘプチル基、5-メチルヘキシル基、2,2-ジメチルペンチル基、3,3-ジメチルペンチル基、4,4-ジメチルペンチル基、1,2-ジメチルペンチル基、1,3-ジメチルペンチル基、1,4-ジメチルペンチル基、1,2,3-トリメチルブチル基、1,1,2-トリメチルブチル基、1,1,3-トリメチルブチル基など）、 $C_1 \sim C_7$ のハロアルキル基（クロロメチル基、ブロモメチル基、ジクロロメチル基、1-クロロエチル基、2-クロロエチル基、3-クロロプロピル基、3-クロロブチル基、5-クロロペンチル基、6-クロロヘキシル基、ジフルオロメチル基、トリフルオロメチル基など）、 $C_2 \sim C_7$ のアルケニル基（ビニル基、アリル基、2-プロペニル基、イソプロペニル基、3-ブテニル基、4-ペンテニル基、5-ヘキセニル基など）、ビスクロ[2, 2, 1]ヘプト-2-イル基、又は $C_3 \sim C_8$ のシクロアルキル基（シクロプロピル基、シクロブチ

ル基、シクロペンチル基、シクロヘキシル基、シクロヘプチル基など)を表し、好ましくは、テトラヒドロフラニル基、 $C_1 \sim C_6$ のアルキル基、 $C_1 \sim C_3$ のハロアルキル基、又は $C_3 \sim C_8$ のシクロアルキル基であり、より好ましくは $C_3 \sim C_8$ のシクロアルキル基、さらに好ましくは $C_4 \sim C_6$ のシクロアルキル基であり、特に好ましくはシクロペンチル基を表す。

Xは水素原子、ハロゲン原子(本明細書においてハロゲンという場合には、フッ素、塩素、臭素、又はヨウ素のいずれでもよい)、又はニトロ基を表し、好ましくは水素原子である。Aとしては、下記の式:



で示される基が好ましい。

上記式中、 R^3 は水素原子、ハロゲン原子、水酸基、 $C_1 \sim C_4$ の直鎖若しくは分岐鎖のアルキル基(メチル基、エチル基、*n*-プロピル基、イソプロピル基、*n*-ブチル基、イソブチル基、*sec*-ブチル基、*t*-ブチル基など)、 $C_1 \sim C_4$ の直鎖若しくは分岐鎖のアルコキシ基(メトキシ基、イソプロポキシ基、ブトキシ基等)、アミノ基、 $C_1 \sim C_4$ の直鎖若しくは分岐鎖のアルキルアミノ基(メチルアミノ基、*n*-プロピルアミノ基、イソプロピルアミノ基、ブチルアミノ基など)、又は $C_2 \sim C_8$ の直鎖若しくは分岐鎖のジアルキルアミノ基(ジメチルアミノ基、ジエチルアミノ基、ジプロピルアミノ基、ジブチルアミノ基等)を表し、好ましくは水素原子、ハロゲン原子、水酸基、 $C_1 \sim C_4$ の直鎖若しくは分岐鎖アルキル基、又は $C_1 \sim C_4$ の直鎖若しくは分岐鎖アルコキシ基を表し、さらに好ましくは、水素原子、 $C_1 \sim C_3$ のアルキル基、 $C_1 \sim C_3$ のアルコキシ基を表す。

上記式中、 R^4 、 R^5 はそれぞれ独立して、水素原子、ハロゲン原子、 $C_1 \sim C_4$ の直鎖若しくは分岐鎖のアルキル基(メチル基、エチル基、*n*-プロピル基、

イソプロピル基、*n*-ブチル基、イソブチル基、*sec*-ブチル基、*t*-ブチル基など)、 $C_1 \sim C_4$ の直鎖若しくは分岐鎖のアルコキシ基(メトキシ基、イソプロポキシ基、ブトキシ基など)、アミノ基、 $C_1 \sim C_4$ の直鎖若しくは分岐鎖のアルキルアミノ基(メチルアミノ基、*n*-プロピルアミノ基、イソプロピルアミノ基、ブチルアミノ基等)、ピロリジニル基、モルホリノ基、 $C_2 \sim C_8$ の直鎖若しくは分岐鎖のジアルキルアミノ基(ジメチルアミノ基、ジエチルアミノ基、ジプロピルアミノ基、ジブチルアミノ基等)、又は $-Y-(CH_2)_n-B$ (Y は $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-N(R^6)-$ (R^6 は水素原子又は $C_1 \sim C_4$ の直鎖又は分岐鎖アルキル基(メチル基、エチル基、*n*-プロピル基、イソプロピル基、*n*-ブチル基、イソブチル基、*sec*-ブチル基、*t*-ブチル基等))を表し、好ましくは $-O-$ を表す。 n は0~4の整数を示し、好ましくは1~3の整数を表す。

B はフェニル基、ナフチル基、又は複素環残基を示す。これらの基は、それぞれその環上に、ハロゲン原子、 $C_1 \sim C_4$ の直鎖又は分岐鎖のアルキル基(メチル基、エチル基、*n*-プロピル基、イソプロピル基、*n*-ブチル基、イソブチル基、*sec*-ブチル基、*t*-ブチル基等)、 $C_1 \sim C_4$ のハロアルキル基(クロロメチル基、ブromoメチル基、ジクロロメチル基、1-クロロエチル基、2-クロロエチル基、3-クロロプロピル基、4-クロロブチル基、ジフルオロメチル基、トリフルオロメチル基)、 $C_1 \sim C_4$ の直鎖又は分岐鎖のアルコキシ基(メトキシ基、イソプロポキシ基、ブトキシ基等)、 $C_1 \sim C_4$ の直鎖又は分岐鎖のハロアルコキシ基(トリフルオロメトキシ基、ジフルオロメトキシ基、2, 2, 2-トリフルオロエトキシ基、3-クロロプロポキシ等)、シアノ基、ニトロ基、アミノ基、ヒドロキシ基、カルボキシ基、 $C_1 \sim C_4$ のアシル基(ホルミル基、アセチル基、プロピオニル基等)、 $C_2 \sim C_4$ のアルコキシカルボニル基(メトキシカルボニル基、エトキシカルボニル基等)、 $C_1 \sim C_4$ の直鎖又は分岐鎖のアルキルアミノ基(メチルアミノ基、イソプロピルアミノ基、ブチルアミノ基等)、及び $C_2 \sim C_8$ の直鎖又は分岐鎖のジアルキルアミノ基(ジメチルアミノ基、ジエチルアミノ基

等) からなる群から選ばれる 1 以上の置換基、好ましくは、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、 $C_1 \sim C_4$ のハロアルコキシ基、カルボキシ基、及び $C_2 \sim C_4$ のアルコキシカルボニル基からなる群から選ばれる 1 以上の置換基を有していてもよい。

複素環残基としては、チエニル基、フリル基、ピロリル基、イミダゾリル基、ピラゾリル基、トリアゾリル基、テトラゾリル基、オキサゾリル基、イソオキサゾリル基、チアゾリル基、イソチアゾリル基、ピロリジニル基、ピリジニル基、ピリダジニル基、ピラジニル基、ピリミジニル基、トリアジニル基、ピペリジニル基、ピペリジノ基、モルホリニル基、モルホリノ基、ピペラジニル基、ベンズイミダゾリル基、インドリル基、キノリル基、ナフチリジニル基、キナゾリニル基等の酸素原子、硫黄原子、窒素原子から選ばれるヘテロ原子を 1～4 個有し、環を構成する原子が 5～10 のもの、好ましくはチエニル基、フリル基、ピロリル基、イミダゾリル基、ピラゾリル基、ピリジニル基、ピリダジニル基、ピラジニル基、ピリミジニル基、トリアジニル基、ピペリジニル基、ピペリジノ基、モルホリニル基、モルホリノ基、ピペラジニル基、ベンズイミダゾリル基さらに好ましくはピリジニル基、ピリダジニル基、ピラジニル基、ピリミジニル基、トリアジニル基、ピペリジニル基、ピペリジノ基、モルホリニル基、モルホリノ基、ピペラジニル基等ヘテロ原子として窒素原子を 1 又は 2 個有する 6 員環の複素環残基を用いることができる。B は好ましくは置換基を有していてもよい複素環残基を表し、特に好ましくは無置換の複素環残基を表す。

R^4 、 R^5 において、好ましくは、 R^4 は水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、 $C_1 \sim C_4$ のアルキルアミノ基又は $C_2 \sim C_8$ のジアルキルアミノ基を表し、さらに好ましくは、 $C_1 \sim C_3$ のアルキル基、 $C_1 \sim C_3$ のアルコキシ基、 $C_1 \sim C_3$ のアルキルアミノ基を表し、 R^5 は $-Y-(CH_2)_n-B$ (Y 、 n 、及び B は既に定義したとおりである) を表す。

ただし、X が水素原子を表す場合には、 R^4 又は R^5 のいずれかは $-Y-(CH_2)_n-B$ を表す。この場合、 Y は $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-N$

(R⁶) - (R⁶は水素原子又はC₁~C₄のアルキル基を表す)を表し、(i) Yが-O-、-S-、又は-NHCO-を表す場合には、nは0~4の整数を表し、Bはそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基を表し、(ii) Yが-N(R⁶)-を表す場合には、nは1~4の整数を表し、Bは複素環残基を表す}で示される基を表す

上記一般式(I)で表される化合物は、R⁴又はR⁵が-Y-(CH₂)_n-Bを表し、Bがヘテロ原子として窒素原子を1つ以上有する複素環残基である場合には、N-オキシド体として存在することもあるが、N-オキシド体も本発明の範囲に包含される。

本発明の化合物の具体例を下記表1に示す。表中、Meはメチル基、Etはエチル基、n-Prはノルマルプロピル基を表す。

表一1








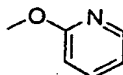

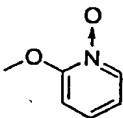

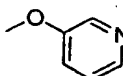

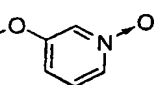

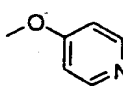

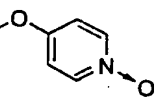

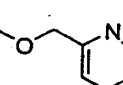

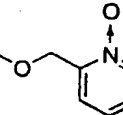
化合物No	X	R1	R2	R3	R4	R5
1	H	Me		H	H	H
2	H	Me		H	H	OMe
3	H	Me		H	H	F
4	H	Me		H	H	Cl
5	H	Me		H	H	Br
6	H	Me		H	H	I
7	H	Me		H	H	
8	H	Me		H	H	
9	H	Me		H	H	
10	H	Me		H	H	
11	H	Me		H	H	
12	H	Me		H	H	
13	H	Me		H	H	
14	H	Me		H	H	

表-1(つづき)


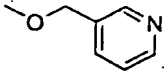

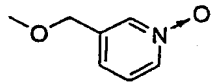

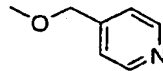

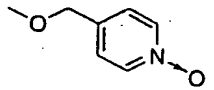

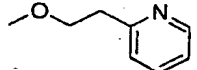

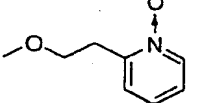

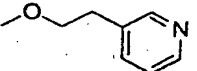

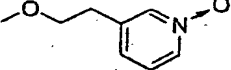

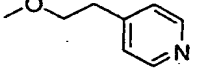

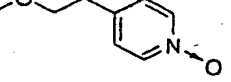

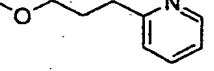

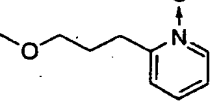

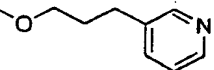

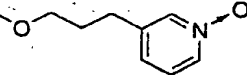
化合物No	X	R1	R2	R3	R4	R5
15	H	Me		H	H	
16	H	Me		H	H	
17	H	Me		H	H	
18	H	Me		H	H	
19	H	Me		H	H	
20	H	Me		H	H	
21	H	Me		H	H	
22	H	Me		H	H	
23	H	Me		H	H	
24	H	Me		H	H	
25	H	Me		H	H	
26	H	Me		H	H	
27	H	Me		H	H	
28	H	Me		H	H	

表-1(つづき)


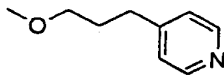

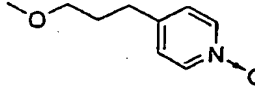

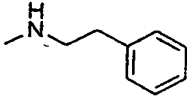

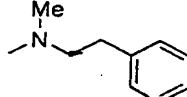

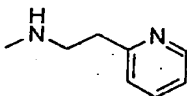

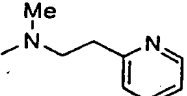

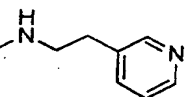

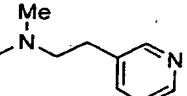

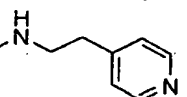

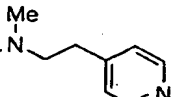

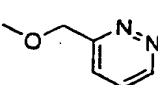

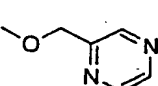

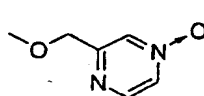

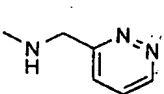
化合物No	X	R1	R2	R3	R4	R5
29	H	Me		H	H	
30	H	Me		H	H	
31	H	Me		H	H	
32	H	Me		H	H	
33	H	Me		H	H	
34	H	Me		H	H	
35	H	Me		H	H	
36	H	Me		H	H	
37	H	Me		H	H	
38	H	Me		H	H	
39	H	Me		H	H	
40	H	Me		H	H	
41	H	Me		H	H	
42	H	Me		H	H	

表-1(つづき)


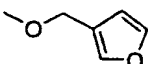

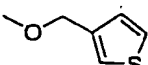

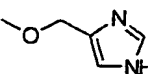

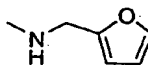

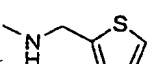

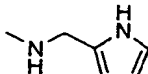

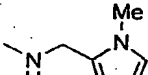

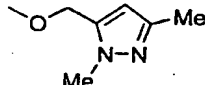






化合物No	X	R1	R2	R3	R4	R5
43	H	Me		H	H	
44	H	Me		H	H	
45	H	Me		H	H	
46	H	Me		H	H	
47	H	Me		H	H	
48	H	Me		H	H	
49	H	Me		H	H	
50	H	Me		H	H	
51	H	Me		H	Me	H
52	H	Me		H	Me	OMe
53	H	Me		H	Me	F
54	H	Me		H	Me	Cl
55	H	Me		H	Me	Br
56	H	Me		H	Me	I

表-1(つづき)


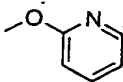

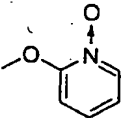

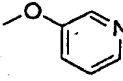

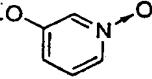

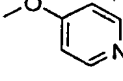

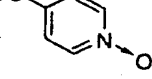

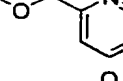

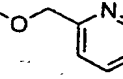

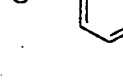

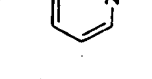

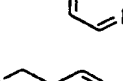

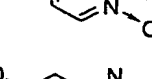

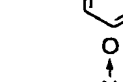

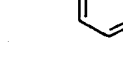

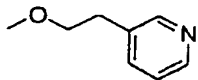

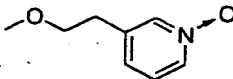

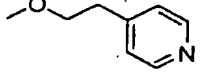

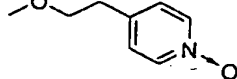

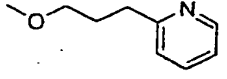

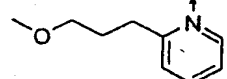

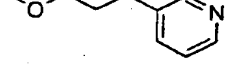

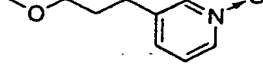





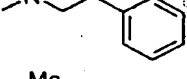

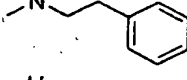

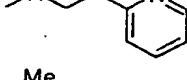

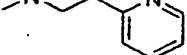
化合物No	X	R1	R2	R3	R4	R5
57	H	Me		H	Me	
58	H	Me		H	Me	
59	H	Me		H	Me	
60	H	Me		H	Me	
61	H	Me		H	Me	
62	H	Me		H	Me	
63	H	Me		H	Me	
64	H	Me		H	Me	
65	H	Me		H	Me	
66	H	Me		H	Me	
67	H	Me		H	Me	
68	H	Me		H	Me	
69	H	Me		H	Me	
70	H	Me		H	Me	

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
71	H	Me		H	Me	
72	H	Me		H	Me	
73	H	Me		H	Me	
74	H	Me		H	Me	
75	H	Me		H	Me	
76	H	Me		H	Me	
77	H	Me		H	Me	
78	H	Me		H	Me	
79	H	Me		H	Me	
80	H	Me		H	Me	
81	H	Me		H	Me	
82	H	Me		H	Me	
83	H	Me		H	Me	
84	H	Me		H	Me	

表一(つづき)


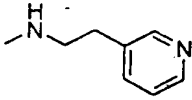

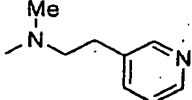

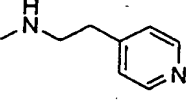

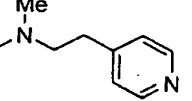

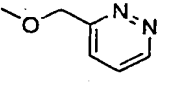

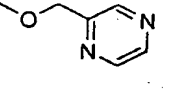

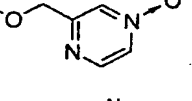

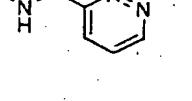

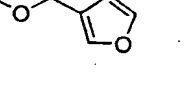

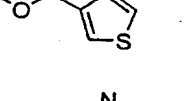

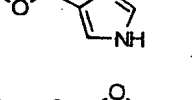

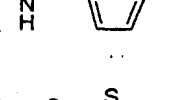

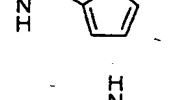

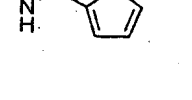

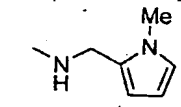

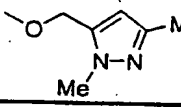







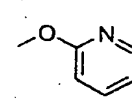

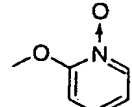

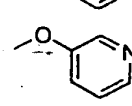

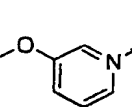

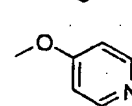

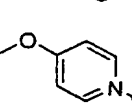
化合物No	X	R1	R2	R3	R4	R5
85	H	Me		H	Me	
86	H	Me		H	Me	
87	H	Me		H	Me	
88	H	Me		H	Me	
89	H	Me		H	Me	
90	H	Me		H	Me	
91	H	Me		H	Me	
92	H	Me		H	Me	
93	H	Me		H	Me	
94	H	Me		H	Me	
95	H	Me		H	Me	
96	H	Me		H	Me	
97	H	Me		H	Me	
98	H	Me		H	Me	

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
99	H	Me		H	Me	
100	H	Me		H	Me	
101	H	Me		H	Et	H
102	H	Me		H	Et	OMe
103	H	Me		H	Et	F
104	H	Me		H	Et	Cl
105	H	Me		H	Et	Br
106	H	Me		H	Et	I
107	H	Me		H	Et	
108	H	Me		H	Et	
109	H	Me		H	Et	
110	H	Me		H	Et	
111	H	Me		H	Et	
112	H	Me		H	Et	

表一1(つづき)


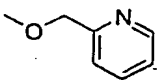

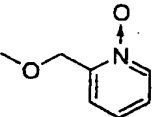

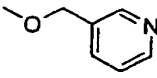

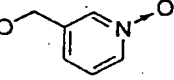

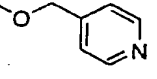

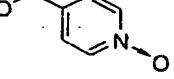

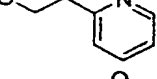

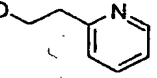

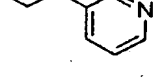

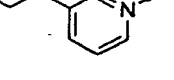

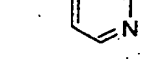

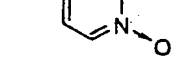

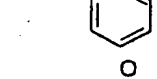

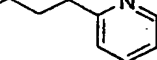

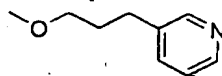

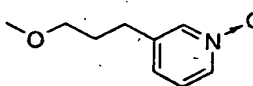

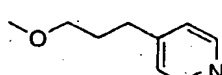

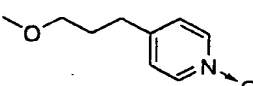

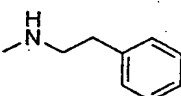

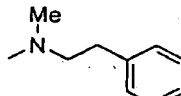

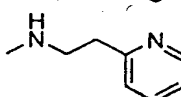

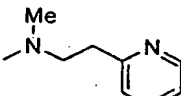

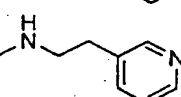

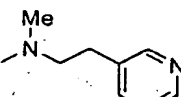

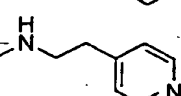

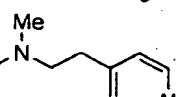

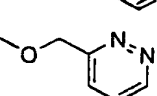

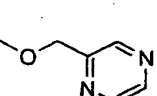

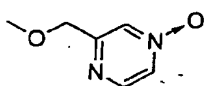

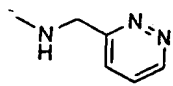

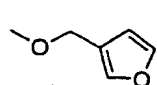

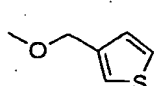

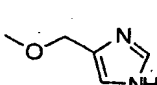

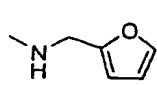

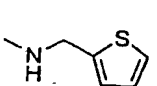

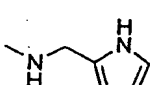

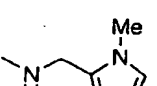

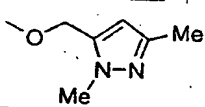




化合物No	X	R1	R2	R3	R4	R5
113	H	Me		H	Et	
114	H	Me		H	Et	
115	H	Me		H	Et	
116	H	Me		H	Et	
117	H	Me		H	Et	
118	H	Me		H	Et	
119	H	Me		H	Et	
120	H	Me		H	Et	
121	H	Me		H	Et	
122	H	Me		H	Et	
123	H	Me		H	Et	
124	H	Me		H	Et	
125	H	Me		H	Et	
126	H	Me		H	Et	




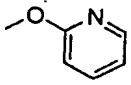

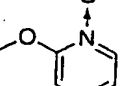

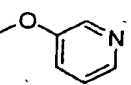

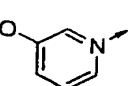

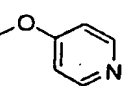

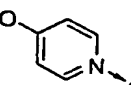

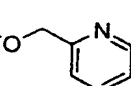

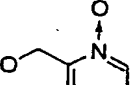

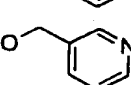

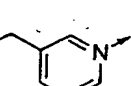

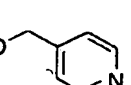

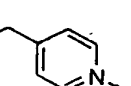
表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
127	H	Me		H	Et	
128	H	Me		H	Et	
129	H	Me		H	Et	
130	H	Me		H	Et	
131	H	Me		H	Et	
132	H	Me		H	Et	
133	H	Me		H	Et	
134	H	Me		H	Et	
135	H	Me		H	Et	
136	H	Me		H	Et	
137	H	Me		H	Et	
138	H	Me		H	Et	
139	H	Me		H	Et	
140	H	Me		H	Et	

表一(つづき)

化合物No	X	R1	R2	R3	R4	R5
141	H	Me		H	Et	
142	H	Me		H	Et	
143	H	Me		H	Et	
144	H	Me		H	Et	
145	H	Me		H	Et	
146	H	Me		H	Et	
147	H	Me		H	Et	
148	H	Me		H	Et	
149	H	Me		H	Et	
150	H	Me		H	Et	
151	H	Me		H	OMe	H
152	H	Me		H	OMe	OMe
153	H	Me		H	OMe	F
154	H	Me		H	OMe	Cl

表一(つづき)

化合物No	X	R1	R2	R3	R4	R5
155	H	Me		H	OMe	Br
156	H	Me		H	OMe	I
157	H	Me		H	OMe	
158	H	Me		H	OMe	
159	H	Me		H	OMe	
160	H	Me		H	OMe	
161	H	Me		H	OMe	
162	H	Me		H	OMe	
163	H	Me		H	OMe	
164	H	Me		H	OMe	
165	H	Me		H	OMe	
166	H	Me		H	OMe	
167	H	Me		H	OMe	
168	H	Me		H	OMe	

表一(つづき)


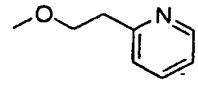

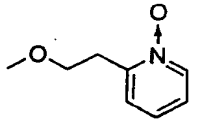

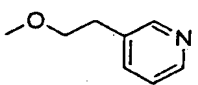

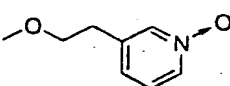

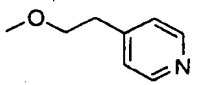

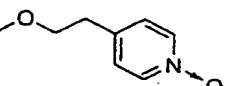

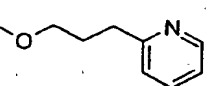

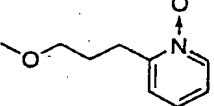

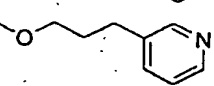

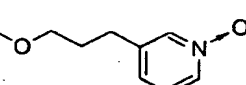

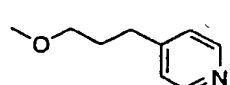

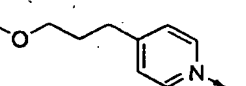

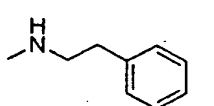

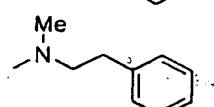
化合物No	X	R1	R2	R3	R4	R5
169	H	Me		H	OMe	
170	H	Me		H	OMe	
171	H	Me		H	OMe	
172	H	Me		H	OMe	
173	H	Me		H	OMe	
174	H	Me		H	OMe	
175	H	Me		H	OMe	
176	H	Me		H	OMe	
177	H	Me		H	OMe	
178	H	Me		H	OMe	
179	H	Me		H	OMe	
180	H	Me		H	OMe	
181	H	Me		H	OMe	
182	H	Me		H	OMe	

表-1(つづき)


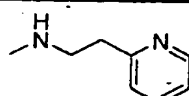

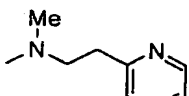

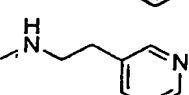

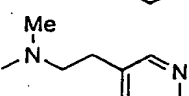

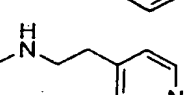

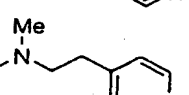

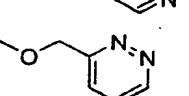

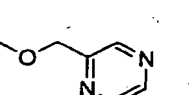

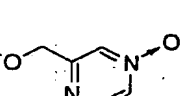

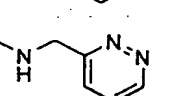

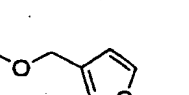

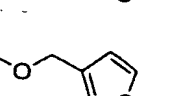

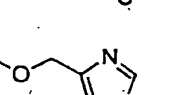

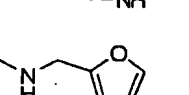

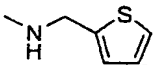

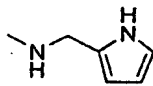

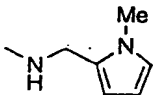

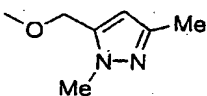







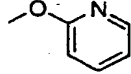

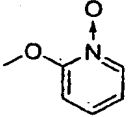

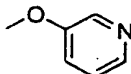

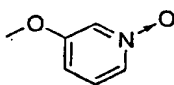

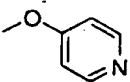

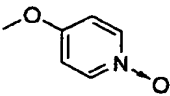

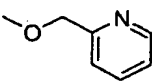

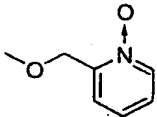

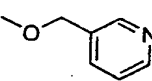

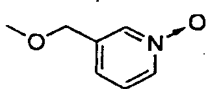

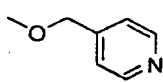

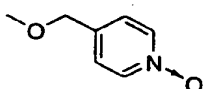

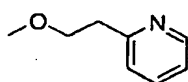

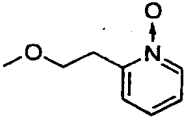

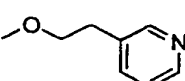

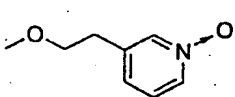

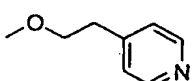

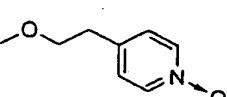
化合物No	X	R1	R2	R3	R4	R5
183	H	Me		H	OMe	
184	H	Me		H	OMe	
185	H	Me		H	OMe	
186	H	Me		H	OMe	
187	H	Me		H	OMe	
188	H	Me		H	OMe	
189	H	Me		H	OMe	
190	H	Me		H	OMe	
191	H	Me		H	OMe	
192	H	Me		H	OMe	
193	H	Me		H	OMe	
194	H	Me		H	OMe	
195	H	Me		H	OMe	
196	H	Me		H	OMe	

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
197	H	Me		H	OMe	
198	H	Me		H	OMe	
199	H	Me		H	OMe	
200	H	Me		H	OMe	
201	H	Me		H	NH ₂	H
202	H	Me		H	NH ₂	OMe
203	H	Me		H	NH ₂	F
204	H	Me		H	NH ₂	Cl
205	H	Me		H	NH ₂	Br
206	H	Me		H	NH ₂	I
207	H	Me		H	NH ₂	
208	H	Me		H	NH ₂	
209	H	Me		H	NH ₂	
210	H	Me		H	NH ₂	

表一(つづき)

化合物No	X	R1	R2	R3	R4	R5
211	H	Me		H	NH ₂	
212	H	Me		H	NH ₂	
213	H	Me		H	NH ₂	
214	H	Me		H	NH ₂	
215	H	Me		H	NH ₂	
216	H	Me		H	NH ₂	
217	H	Me		H	NH ₂	
218	H	Me		H	NH ₂	
219	H	Me		H	NH ₂	
220	H	Me		H	NH ₂	
221	H	Me		H	NH ₂	
222	H	Me		H	NH ₂	
223	H	Me		H	NH ₂	
224	H	Me		H	NH ₂	

表一(つづき)


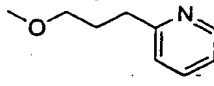

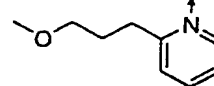

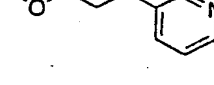

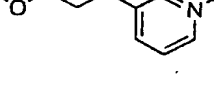

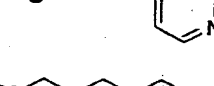

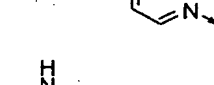

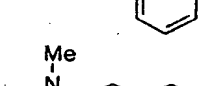

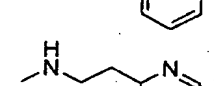

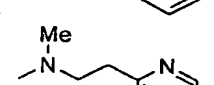

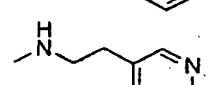

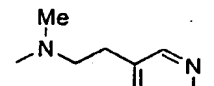

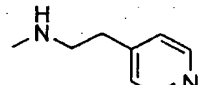

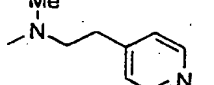



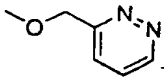

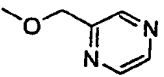

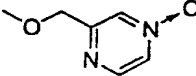

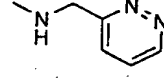

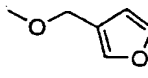

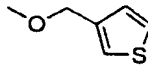

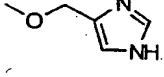

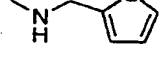

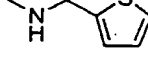

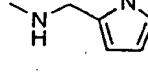

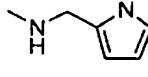

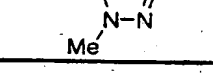







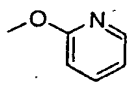

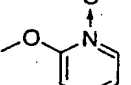

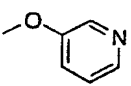

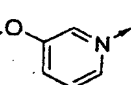

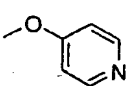

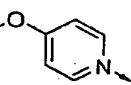

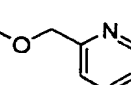

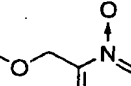

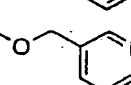

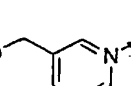
化合物No	X	R1	R2	R3	R4	R5
225	H	Me		H	NH ₂	
226	H	Me		H	NH ₂	
227	H	Me		H	NH ₂	
228	H	Me		H	NH ₂	
229	H	Me		H	NH ₂	
230	H	Me		H	NH ₂	
231	H	Me		H	NH ₂	
232	H	Me		H	NH ₂	
233	H	Me		H	NH ₂	
234	H	Me		H	NH ₂	
235	H	Me		H	NH ₂	
236	H	Me		H	NH ₂	
237	H	Me		H	NH ₂	
238	H	Me		H	NH ₂	


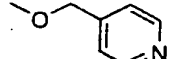

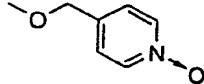

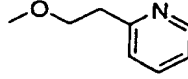

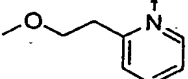

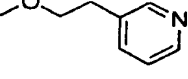

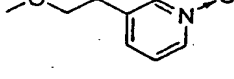



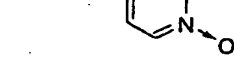







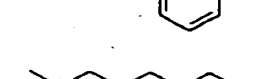

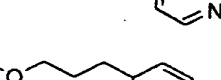


表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
239	H	Me		H	NH ₂	
240	H	Me		H	NH ₂	
241	H	Me		H	NH ₂	
242	H	Me		H	NH ₂	
243	H	Me		H	NH ₂	
244	H	Me		H	NH ₂	
245	H	Me		H	NH ₂	
246	H	Me		H	NH ₂	
247	H	Me		H	NH ₂	
248	H	Me		H	NH ₂	
249	H	Me		H	NH ₂	
250	H	Me		H	NH ₂	
251	H	Me		H	NHMe	H
252	H	Me		H	NHMe	OMe

表一(つづき)

化合物No	X	R1	R2	R3	R4	R5
253	H	Me		H	NHMe	F
254	H	Me		H	NHMe	Cl
255	H	Me		H	NHMe	Br
256	H	Me		H	NHMe	I
257	H	Me		H	NHMe	
258	H	Me		H	NHMe	
259	H	Me		H	NHMe	
260	H	Me		H	NHMe	
261	H	Me		H	NHMe	
262	H	Me		H	NHMe	
263	H	Me		H	NHMe	
264	H	Me		H	NHMe	
265	H	Me		H	NHMe	
266	H	Me		H	NHMe	

表一(つづき)

化合物No	X	R1	R2	R3	R4	R5
267	H	Me		H	NHMe	
268	H	Me		H	NHMe	
269	H	Me		H	NHMe	
270	H	Me		H	NHMe	
271	H	Me		H	NHMe	
272	H	Me		H	NHMe	
273	H	Me		H	NHMe	
274	H	Me		H	NHMe	
275	H	Me		H	NHMe	
276	H	Me		H	NHMe	
277	H	Me		H	NHMe	
278	H	Me		H	NHMe	
279	H	Me		H	NHMe	
280	H	Me		H	NHMe	

表一(つづき)


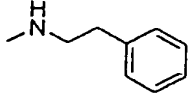

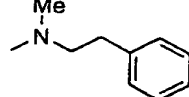

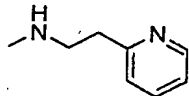

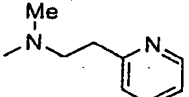

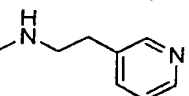

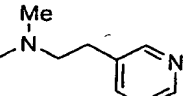

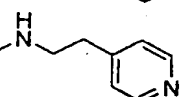

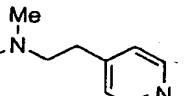

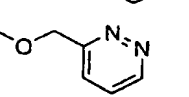

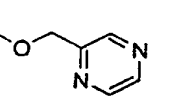

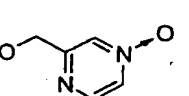

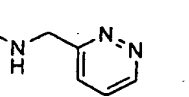

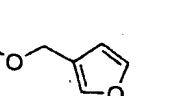

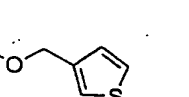
化合物No	X	R1	R2	R3	R4	R5
281	H	Me		H	NHMe	
282	H	Me		H	NHMe	
283	H	Me		H	NHMe	
284	H	Me		H	NHMe	
285	H	Me		H	NHMe	
286	H	Me		H	NHMe	
287	H	Me		H	NHMe	
288	H	Me		H	NHMe	
289	H	Me		H	NHMe	
290	H	Me		H	NHMe	
291	H	Me		H	NHMe	
292	H	Me		H	NHMe	
293	H	Me		H	NHMe	
294	H	Me		H	NHMe	

表-1(つづき)


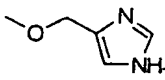

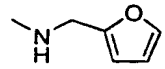

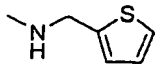

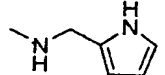

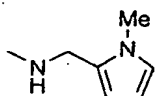

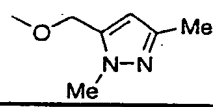







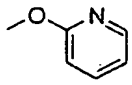

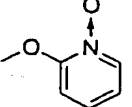
化合物No	X	R1	R2	R3	R4	R5
295	H	Me		H	NHMe	
296	H	Me		H	NHMe	
297	H	Me		H	NHMe	
298	H	Me		H	NHMe	
299	H	Me		H	NHMe	
300	H	Me		H	NHMe	
301	H	Me		H	NHEt	H
302	H	Me		H	NHEt	OMe
303	H	Me		H	NHEt	F
304	H	Me		H	NHEt	Cl
305	H	Me		H	NHEt	Br
306	H	Me		H	NHEt	I
307	H	Me		H	NHEt	
308	H	Me		H	NHEt	

表-1(つづき)


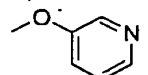

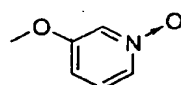

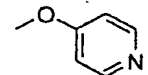

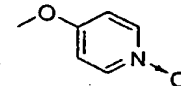

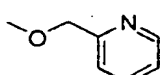

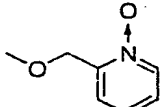

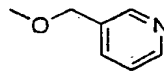

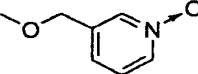

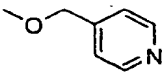

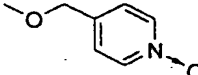

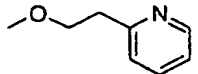

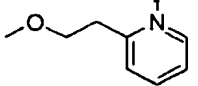

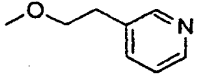

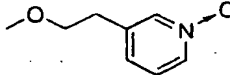
化合物No	X	R1	R2	R3	R4	R5
309	H	Me		H	NHEt	
310	H	Me		H	NHEt	
311	H	Me		H	NHEt	
312	H	Me		H	NHEt	
313	H	Me		H	NHEt	
314	H	Me		H	NHEt	
315	H	Me		H	NHEt	
316	H	Me		H	NHEt	
317	H	Me		H	NHEt	
318	H	Me		H	NHEt	
319	H	Me		H	NHEt	
320	H	Me		H	NHEt	
321	H	Me		H	NHEt	
322	H	Me		H	NHEt	

表-1(つづき)


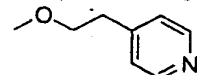

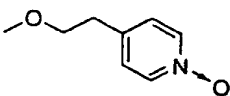

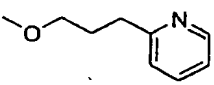

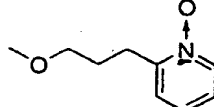

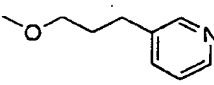

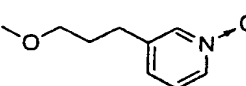

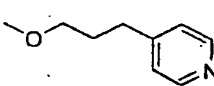

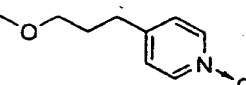

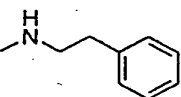

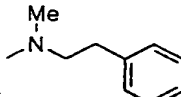

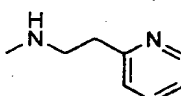

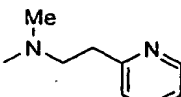

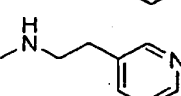

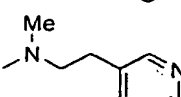

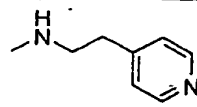

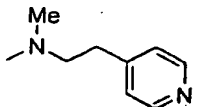

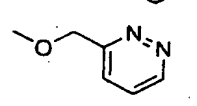

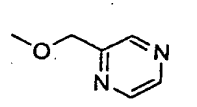

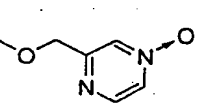

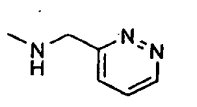

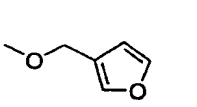

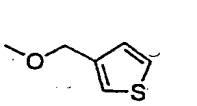

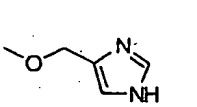

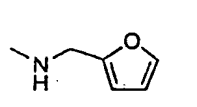

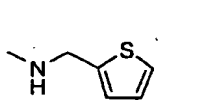

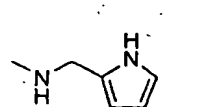

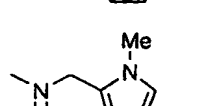

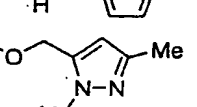
化合物No	X	R1	R2	R3	R4	R5
323	H	Me		H	NHEt	
324	H	Me		H	NHEt	
325	H	Me		H	NHEt	
326	H	Me		H	NHEt	
327	H	Me		H	NHEt	
328	H	Me		H	NHEt	
329	H	Me		H	NHEt	
330	H	Me		H	NHEt	
331	H	Me		H	NHEt	
332	H	Me		H	NHEt	
333	H	Me		H	NHEt	
334	H	Me		H	NHEt	
335	H	Me		H	NHEt	
336	H	Me		H	NHEt	

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
337	H	Me		H	NHEt	
338	H	Me		H	NHEt	
339	H	Me		H	NHEt	
340	H	Me		H	NHEt	
341	H	Me		H	NHEt	
342	H	Me		H	NHEt	
343	H	Me		H	NHEt	
344	H	Me		H	NHEt	
345	H	Me		H	NHEt	
346	H	Me		H	NHEt	
347	H	Me		H	NHEt	
348	H	Me		H	NHEt	
349	H	Me		H	NHEt	
350	H	Me		H	NHEt	

表一(つづき)








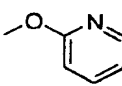

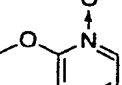

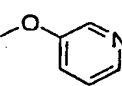

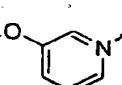

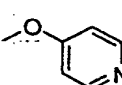

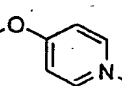

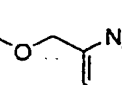

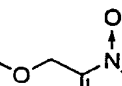
化合物No	X	R1	R2	R3	R4	R5
351	H	Me		H	NH <i>n</i> -Pr	H
352	H	Me		H	NH <i>n</i> -Pr	OMe
353	H	Me		H	NH <i>n</i> -Pr	F
354	H	Me		H	NH <i>n</i> -Pr	Cl
355	H	Me		H	NH <i>n</i> -Pr	Br
356	H	Me		H	NH <i>n</i> -Pr	I
357	H	Me		H	NH <i>n</i> -Pr	
358	H	Me		H	NH <i>n</i> -Pr	
359	H	Me		H	NH <i>n</i> -Pr	
360	H	Me		H	NH <i>n</i> -Pr	
361	H	Me		H	NH <i>n</i> -Pr	
362	H	Me		H	NH <i>n</i> -Pr	
363	H	Me		H	NH <i>n</i> -Pr	
364	H	Me		H	NH <i>n</i> -Pr	

表-1(つづき)


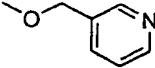

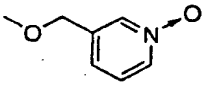

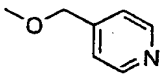

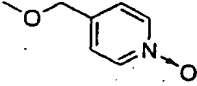

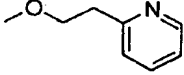

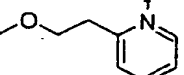

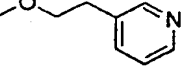

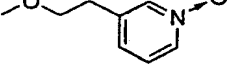

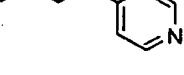

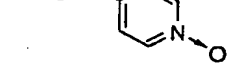

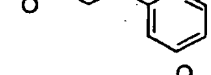

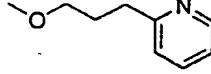



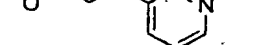
化合物No	X	R1	R2	R3	R4	R5
365	H	Me		H	NH <i>n</i> -Pr	
366	H	Me		H	NH <i>n</i> -Pr	
367	H	Me		H	NH <i>n</i> -Pr	
368	H	Me		H	NH <i>n</i> -Pr	
369	H	Me		H	NH <i>n</i> -Pr	
370	H	Me		H	NH <i>n</i> -Pr	
371	H	Me		H	NH <i>n</i> -Pr	
372	H	Me		H	NH <i>n</i> -Pr	
373	H	Me		H	NH <i>n</i> -Pr	
374	H	Me		H	NH <i>n</i> -Pr	
375	H	Me		H	NH <i>n</i> -Pr	
376	H	Me		H	NH <i>n</i> -Pr	
377	H	Me		H	NH <i>n</i> -Pr	
378	H	Me		H	NH <i>n</i> -Pr	

表-1(つづき)


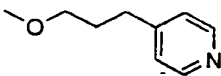

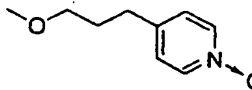

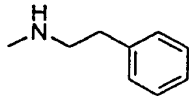

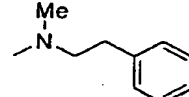

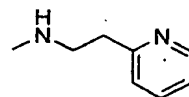

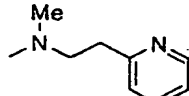

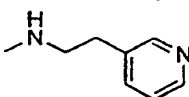

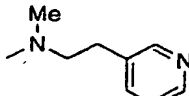

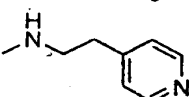

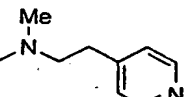

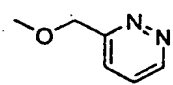

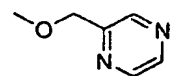

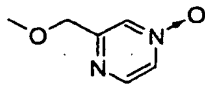

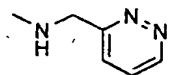
化合物No	X	R1	R2	R3	R4	R5
379	H	Me		H	NH <i>n</i> -Pr	
380	H	Me		H	NH <i>n</i> -Pr	
381	H	Me		H	NH <i>n</i> -Pr	
382	H	Me		H	NH <i>n</i> -Pr	
383	H	Me		H	NH <i>n</i> -Pr	
384	H	Me		H	NH <i>n</i> -Pr	
385	H	Me		H	NH <i>n</i> -Pr	
386	H	Me		H	NH <i>n</i> -Pr	
387	H	Me		H	NH <i>n</i> -Pr	
388	H	Me		H	NH <i>n</i> -Pr	
389	H	Me		H	NH <i>n</i> -Pr	
390	H	Me		H	NH <i>n</i> -Pr	
391	H	Me		H	NH <i>n</i> -Pr	
392	H	Me		H	NH <i>n</i> -Pr	

表-1(つづき)


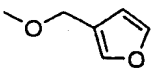

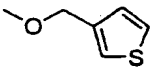

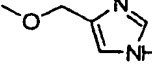

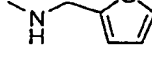

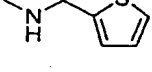

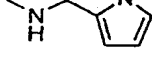

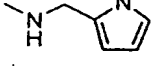

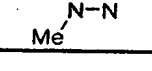






化合物No	X	R1	R2	R3	R4	R5
393	H	Me		H	NH <i>n</i> -Pr	
394	H	Me		H	NH <i>n</i> -Pr	
395	H	Me		H	NH <i>n</i> -Pr	
396	H	Me		H	NH <i>n</i> -Pr	
397	H	Me		H	NH <i>n</i> -Pr	
398	H	Me		H	NH <i>n</i> -Pr	
399	H	Me		H	NH <i>n</i> -Pr	
400	H	Me		H	NH <i>n</i> -Pr	
401	H	Me		H	NMe ₂	H
402	H	Me		H	NMe ₂	OMe
403	H	Me		H	NMe ₂	F
404	H	Me		H	NMe ₂	Cl
405	H	Me		H	NMe ₂	Br
406	H	Me		H	NMe ₂	I

表-1(つづき)


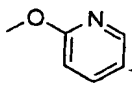

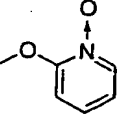

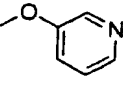

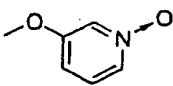

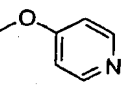

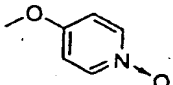

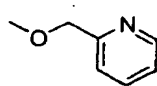

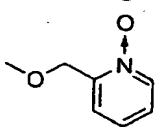

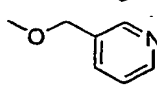

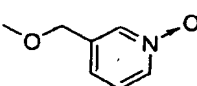

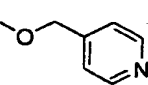

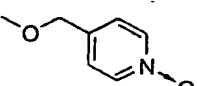

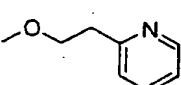

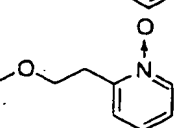
化合物No	X	R1	R2	R3	R4	R5
407	H	Me		H	NMe ₂	
408	H	Me		H	NMe ₂	
409	H	Me		H	NMe ₂	
410	H	Me		H	NMe ₂	
411	H	Me		H	NMe ₂	
412	H	Me		H	NMe ₂	
413	H	Me		H	NMe ₂	
414	H	Me		H	NMe ₂	
415	H	Me		H	NMe ₂	
416	H	Me		H	NMe ₂	
417	H	Me		H	NMe ₂	
418	H	Me		H	NMe ₂	
419	H	Me		H	NMe ₂	
420	H	Me		H	NMe ₂	

表-1(つづき)


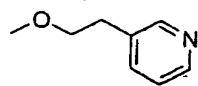

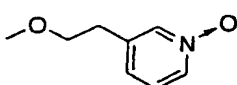

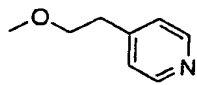

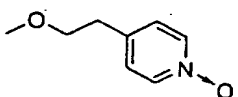

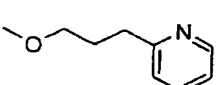

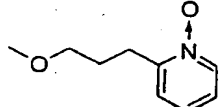

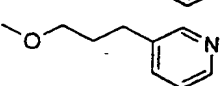

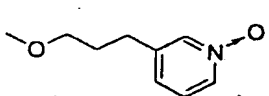

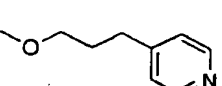

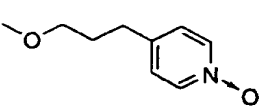

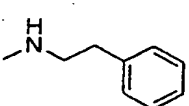

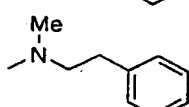

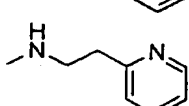

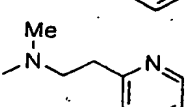
化合物No	X	R1	R2	R3	R4	R5
421	H	Me		H	NMe ₂	
422	H	Me		H	NMe ₂	
423	H	Me		H	NMe ₂	
424	H	Me		H	NMe ₂	
425	H	Me		H	NMe ₂	
426	H	Me		H	NMe ₂	
427	H	Me		H	NMe ₂	
428	H	Me		H	NMe ₂	
429	H	Me		H	NMe ₂	
430	H	Me		H	NMe ₂	
431	H	Me		H	NMe ₂	
432	H	Me		H	NMe ₂	
433	H	Me		H	NMe ₂	
434	H	Me		H	NMe ₂	

表-1(つづき)


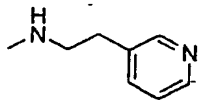

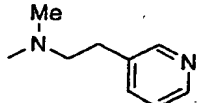

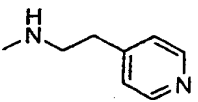

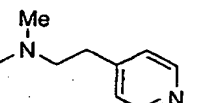

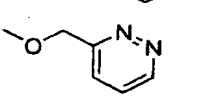

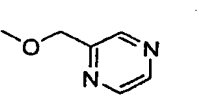

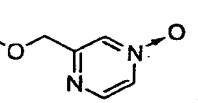

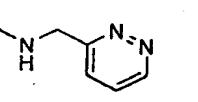

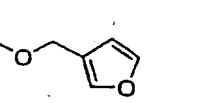

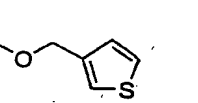

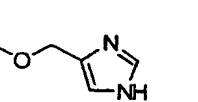

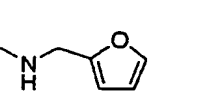

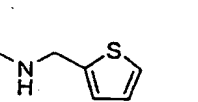

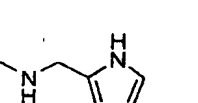
化合物No	X	R1	R2	R3	R4	R5
435	H	Me		H	NMe ₂	
436	H	Me		H	NMe ₂	
437	H	Me		H	NMe ₂	
438	H	Me		H	NMe ₂	
439	H	Me		H	NMe ₂	
440	H	Me		H	NMe ₂	
441	H	Me		H	NMe ₂	
442	H	Me		H	NMe ₂	
443	H	Me		H	NMe ₂	
444	H	Me		H	NMe ₂	
445	H	Me		H	NMe ₂	
446	H	Me		H	NMe ₂	
447	H	Me		H	NMe ₂	
448	H	Me		H	NMe ₂	

表-1(つづき)


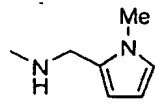

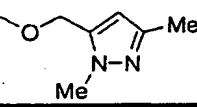







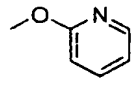

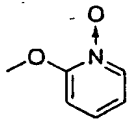

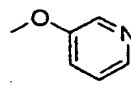

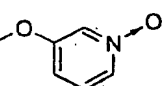

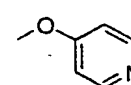

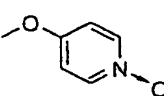
化合物No	X	R1	R2	R3	R4	R5
449	H	Me		H	NMe ₂	
450	H	Me		H	NMe ₂	
451	H	Me		H	Cl	H
452	H	Me		H	Cl	OMe
453	H	Me		H	Cl	F
454	H	Me		H	Cl	Cl
455	H	Me		H	Cl	Br
456	H	Me		H	Cl	I
457	H	Me		H	Cl	
458	H	Me		H	Cl	
459	H	Me		H	Cl	
460	H	Me		H	Cl	
461	H	Me		H	Cl	
462	H	Me		H	Cl	

表-1(つづき)


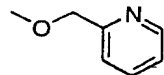

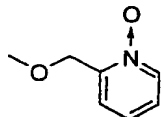

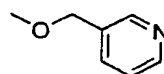

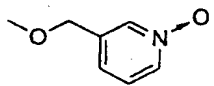

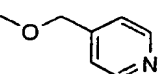

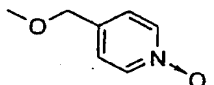

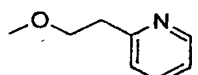

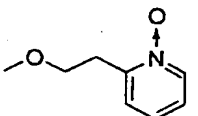

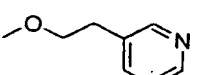

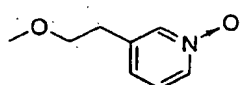

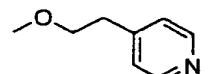

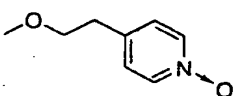

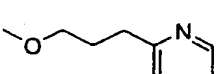

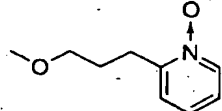

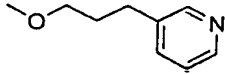

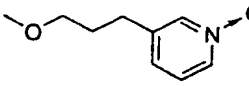

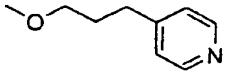

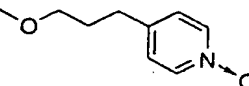

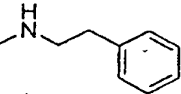

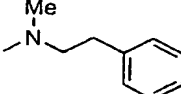

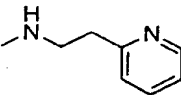

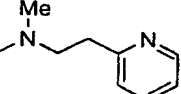

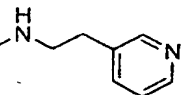

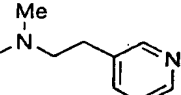

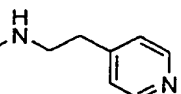

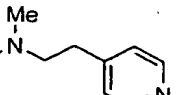

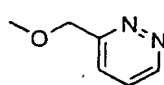

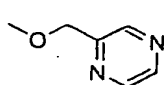
化合物No	X	R1	R2	R3	R4	R5
463	H	Me		H	Cl	
464	H	Me		H	Cl	
465	H	Me		H	Cl	
466	H	Me		H	Cl	
467	H	Me		H	Cl	
468	H	Me		H	Cl	
469	H	Me		H	Cl	
470	H	Me		H	Cl	
471	H	Me		H	Cl	
472	H	Me		H	Cl	
473	H	Me		H	Cl	
474	H	Me		H	Cl	
475	H	Me		H	Cl	
476	H	Me		H	Cl	

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
477	H	Me		H	Cl	
478	H	Me		H	Cl	
479	H	Me		H	Cl	
480	H	Me		H	Cl	
481	H	Me		H	Cl	
482	H	Me		H	Cl	
483	H	Me		H	Cl	
484	H	Me		H	Cl	
485	H	Me		H	Cl	
486	H	Me		H	Cl	
487	H	Me		H	Cl	
488	H	Me		H	Cl	
489	H	Me		H	Cl	
490	H	Me		H	Cl	

表一(つづき)


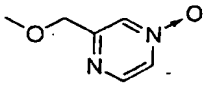

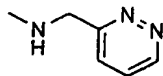

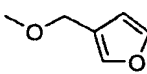

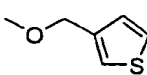

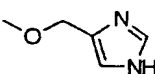

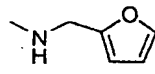

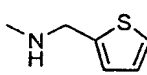

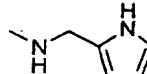

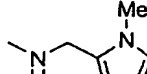

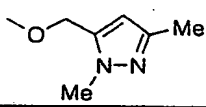








化合物No	X	R1	R2	R3	R4	R5
491	H	Me		H	Cl	
492	H	Me		H	Cl	
493	H	Me		H	Cl	
494	H	Me		H	Cl	
495	H	Me		H	Cl	
496	H	Me		H	Cl	
497	H	Me		H	Cl	
498	H	Me		H	Cl	
499	H	Me		H	Cl	
500	H	Me		H	Cl	
501	H	Me		H		H
502	H	Me		H		OMe
503	H	Me		H		F
504	H	Me		H		Cl

表-1(つづき)







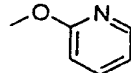


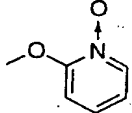


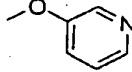


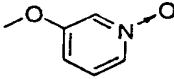


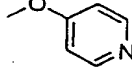


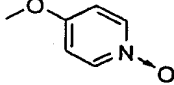


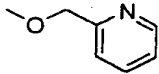


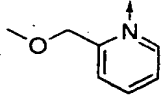


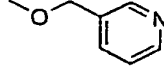


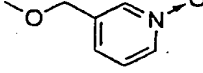


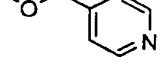


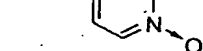
化合物No	X	R1	R2	R3	R4	R5
505	H	Me		H		Br
506	H	Me		H		I
507	H	Me		H		
508	H	Me		H		
509	H	Me		H		
510	H	Me		H		
511	H	Me		H		
512	H	Me		H		
513	H	Me		H		
514	H	Me		H		
515	H	Me		H		
516	H	Me		H		
517	H	Me		H		
518	H	Me		H		

表-1(つづき)



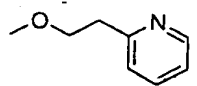


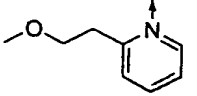


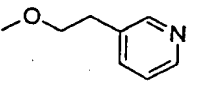


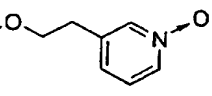


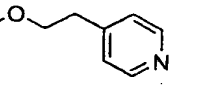


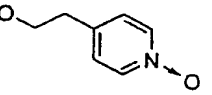


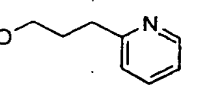


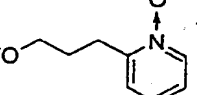


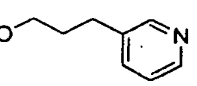


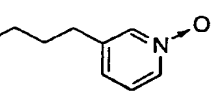


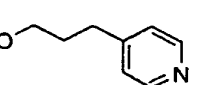


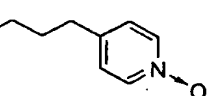


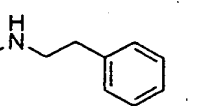


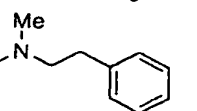


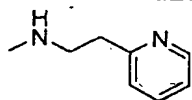


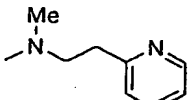


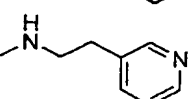


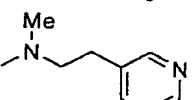


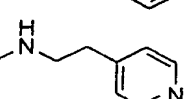


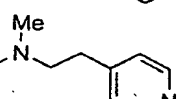


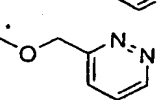


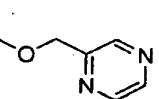


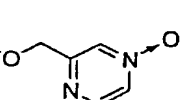


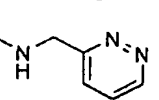


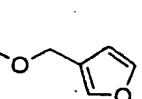


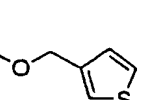


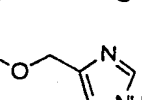


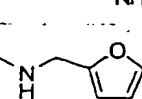
化合物No	X	R1	R2	R3	R4	R5
519	H	Me		H		
520	H	Me		H		
521	H	Me		H		
522	H	Me		H		
523	H	Me		H		
524	H	Me		H		
525	H	Me		H		
526	H	Me		H		
527	H	Me		H		
528	H	Me		H		
529	H	Me		H		
530	H	Me		H		
531	H	Me		H		
532	H	Me		H		

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
533	H	Me		H		
534	H	Me		H		
535	H	Me		H		
536	H	Me		H		
537	H	Me		H		
538	H	Me		H		
539	H	Me		H		
540	H	Me		H		
541	H	Me		H		
542	H	Me		H		
543	H	Me		H		
544	H	Me		H		
545	H	Me		H		
546	H	Me		H		

表一(つづき)



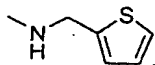


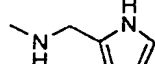


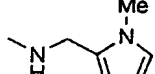


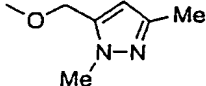

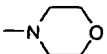

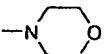

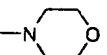

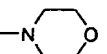

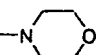

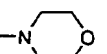


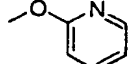


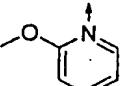

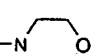
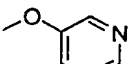

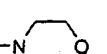
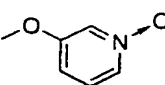
化合物No	X	R1	R2	R3	R4	R5
547	H	Me		H		
548	H	Me		H		
549	H	Me		H		
550	H	Me		H		
551	H	Me		H		H
552	H	Me		H		OMe
553	H	Me		H		F
554	H	Me		H		Cl
555	H	Me		H		Br
556	H	Me		H		I
557	H	Me		H		
558	H	Me		H		
559	H	Me		H		
560	H	Me		H		

表-1(つづき)



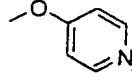


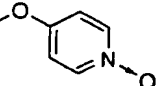


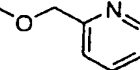


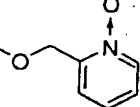


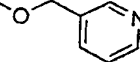


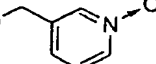


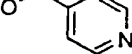


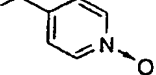





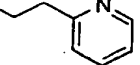


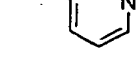


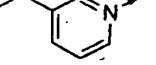


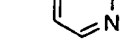


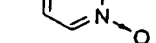
化合物No	X	R1	R2	R3	R4	R5
561	H	Me		H		
562	H	Me		H		
563	H	Me		H		
564	H	Me		H		
565	H	Me		H		
566	H	Me		H		
567	H	Me		H		
568	H	Me		H		
569	H	Me		H		
570	H	Me		H		
571	H	Me		H		
572	H	Me		H		
573	H	Me		H		
574	H	Me		H		

表-1(つづき)


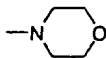
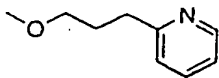

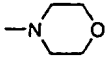
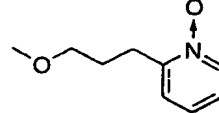

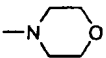
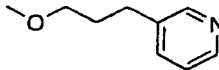

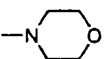
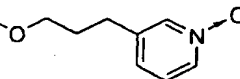

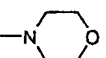
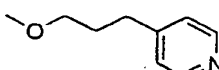

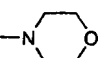
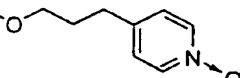

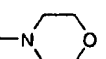
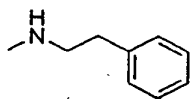

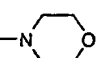
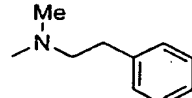

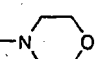
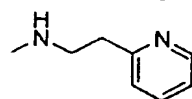

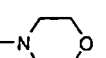
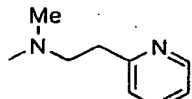

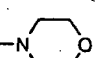
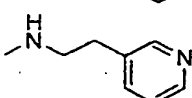

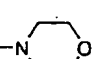
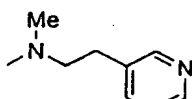

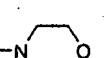
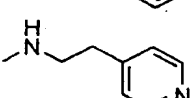

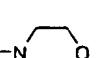
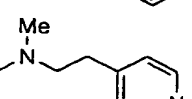
化合物No	X	R1	R2	R3	R4	R5
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576	H	Me		H		
577	H	Me		H		
578	H	Me		H		
579	H	Me		H		
580	H	Me		H		
581	H	Me		H		
582	H	Me		H		
583	H	Me		H		
584	H	Me		H		
585	H	Me		H		
586	H	Me		H		
587	H	Me		H		
588	H	Me		H		

表-1(つづき)


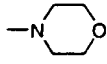
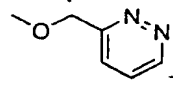

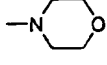
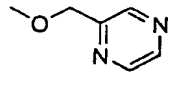

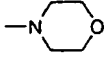
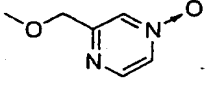

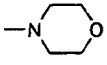
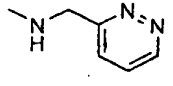

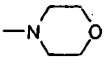
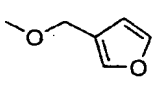

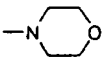
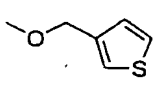

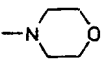
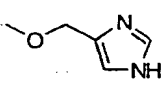

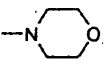
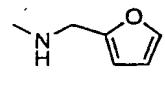

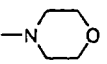
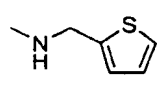

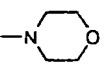
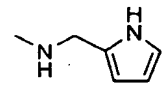

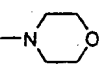
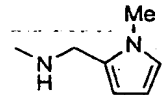

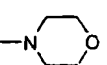
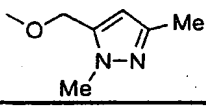







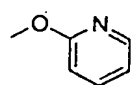

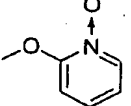

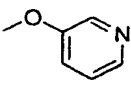

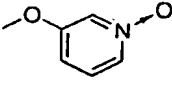

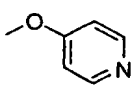

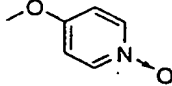

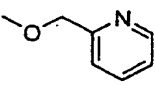

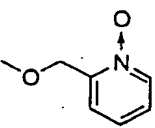

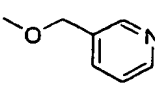

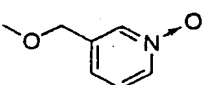

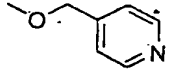

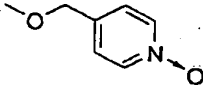

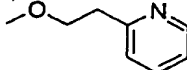

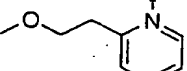

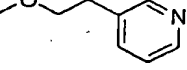

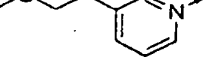

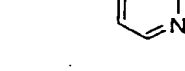

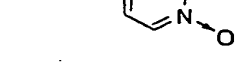



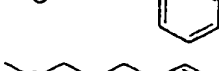



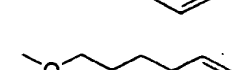

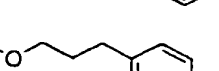


化合物No	X	R1	R2	R3	R4	R5
589	H	Me		H		
590	H	Me		H		
591	H	Me		H		
592	H	Me		H		
593	H	Me		H		
594	H	Me		H		
595	H	Me		H		
596	H	Me		H		
597	H	Me		H		
598	H	Me		H		
599	H	Me		H		
600	H	Me		H		
601	H	Me		Me	H	H
602	H	Me		Me	H	OMe

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
603	H	Me		Me	H	F
604	H	Me		Me	H	Cl
605	H	Me		Me	H	Br
606	H	Me		Me	H	I
607	H	Me		Me	H	
608	H	Me		Me	H	
609	H	Me		Me	H	
610	H	Me		Me	H	
611	H	Me		Me	H	
612	H	Me		Me	H	
613	H	Me		Me	H	
614	H	Me		Me	H	
615	H	Me		Me	H	
616	H	Me		Me	H	

表一(つづき)

化合物No	X	R1	R2	R3	R4	R5
617	H	Me		Me	H	
618	H	Me		Me	H	
619	H	Me		Me	H	
620	H	Me		Me	H	
621	H	Me		Me	H	
622	H	Me		Me	H	
623	H	Me		Me	H	
624	H	Me		Me	H	
625	H	Me		Me	H	
626	H	Me		Me	H	
627	H	Me		Me	H	
628	H	Me		Me	H	
629	H	Me		Me	H	
630	H	Me		Me	H	

表一1(つづき)


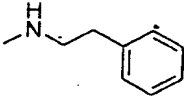

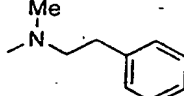

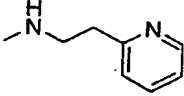

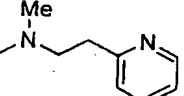

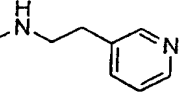

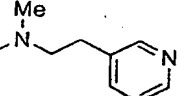

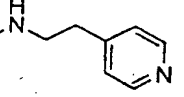

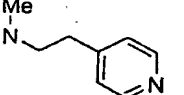

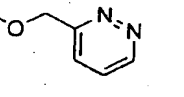

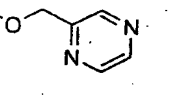

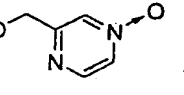

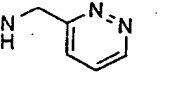

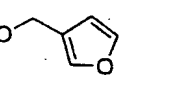

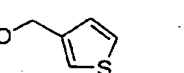
化合物No	X	R1	R2	R3	R4	R5
631	H	Me		Me	H	
632	H	Me		Me	H	
633	H	Me		Me	H	
634	H	Me		Me	H	
635	H	Me		Me	H	
636	H	Me		Me	H	
637	H	Me		Me	H	
638	H	Me		Me	H	
639	H	Me		Me	H	
640	H	Me		Me	H	
641	H	Me		Me	H	
642	H	Me		Me	H	
643	H	Me		Me	H	
644	H	Me		Me	H	

表-1(つづき)


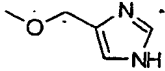

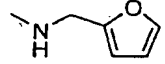

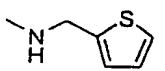

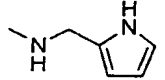

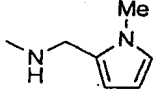

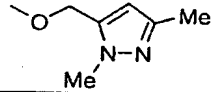







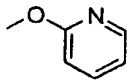

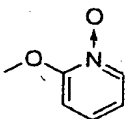
化合物No	X	R1	R2	R3	R4	R5
645	H	Me		Me	H	
646	H	Me		Me	H	
647	H	Me		Me	H	
648	H	Me		Me	H	
649	H	Me		Me	H	
650	H	Me		Me	H	
651	H	Me		Me	Me	H
652	H	Me		Me	Me	OMe
653	H	Me		Me	Me	F
654	H	Me		Me	Me	Cl
655	H	Me		Me	Me	Br
656	H	Me		Me	Me	I
657	H	Me		Me	Me	
658	H	Me		Me	Me	

表-1(つづき)


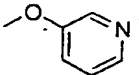

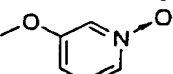

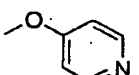

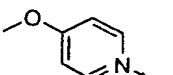

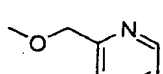

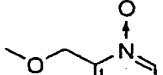

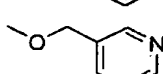

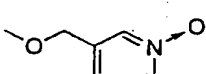

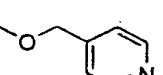

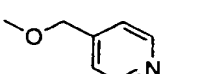

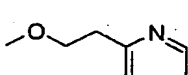

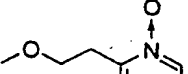

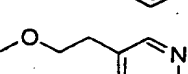

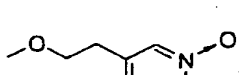

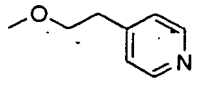

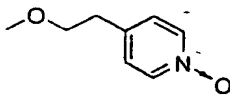

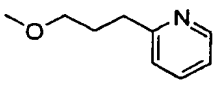

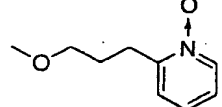

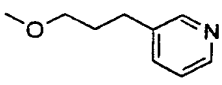

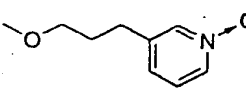

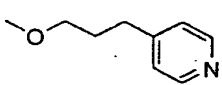

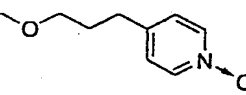

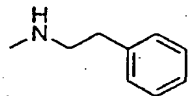

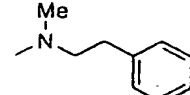

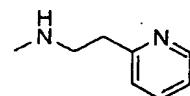

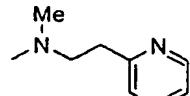

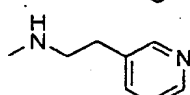

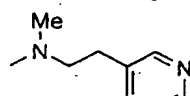
化合物No	X	R1	R2	R3	R4	R5
659	H	Me		Me	Me	
660	H	Me		Me	Me	
661	H	Me		Me	Me	
662	H	Me		Me	Me	
663	H	Me		Me	Me	
664	H	Me		Me	Me	
665	H	Me		Me	Me	
666	H	Me		Me	Me	
667	H	Me		Me	Me	
668	H	Me		Me	Me	
669	H	Me		Me	Me	
670	H	Me		Me	Me	
671	H	Me		Me	Me	
672	H	Me		Me	Me	

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
673	H	Me		Me	Me	
674	H	Me		Me	Me	
675	H	Me		Me	Me	
676	H	Me		Me	Me	
677	H	Me		Me	Me	
678	H	Me		Me	Me	
679	H	Me		Me	Me	
680	H	Me		Me	Me	
681	H	Me		Me	Me	
682	H	Me		Me	Me	
683	H	Me		Me	Me	
684	H	Me		Me	Me	
685	H	Me		Me	Me	
686	H	Me		Me	Me	

表一(つづき)


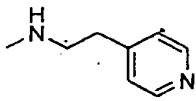

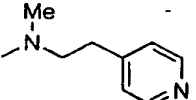

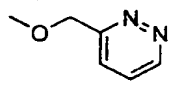

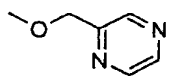

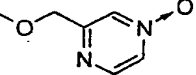

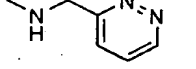

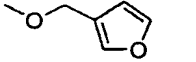

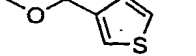

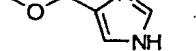









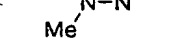
化合物No	X	R1	R2	R3	R4	R5
687	H	Me		Me	Me	
688	H	Me		Me	Me	
689	H	Me		Me	Me	
690	H	Me		Me	Me	
691	H	Me		Me	Me	
692	H	Me		Me	Me	
693	H	Me		Me	Me	
694	H	Me		Me	Me	
695	H	Me		Me	Me	
696	H	Me		Me	Me	
697	H	Me		Me	Me	
698	H	Me		Me	Me	
699	H	Me		Me	Me	
700	H	Me		Me	Me	

表-1(つづき)








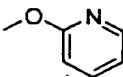

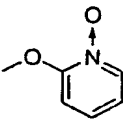

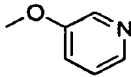

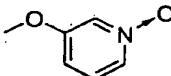

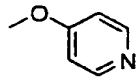

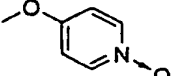

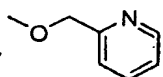

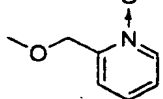
化合物No	X	R1	R2	R3	R4	R5
701	H	Me		Me	Et	H
702	H	Me		Me	Et	OMe
703	H	Me		Me	Et	F
704	H	Me		Me	Et	Cl
705	H	Me		Me	Et	Br
706	H	Me		Me	Et	I
707	H	Me		Me	Et	
708	H	Me		Me	Et	
709	H	Me		Me	Et	
710	H	Me		Me	Et	
711	H	Me		Me	Et	
712	H	Me		Me	Et	
713	H	Me		Me	Et	
714	H	Me		Me	Et	

表-1(つづき)


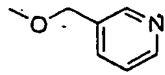

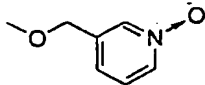

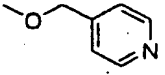

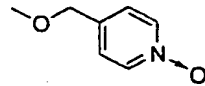

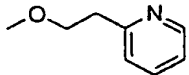

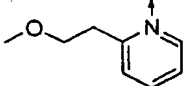

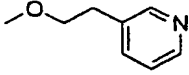

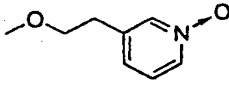

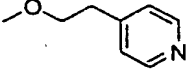

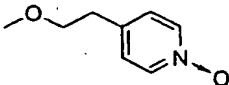

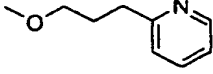

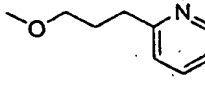



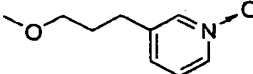
化合物No	X	R1	R2	R3	R4	R5
715	H	Me		Me	Et	
716	H	Me		Me	Et	
717	H	Me		Me	Et	
718	H	Me		Me	Et	
719	H	Me		Me	Et	
720	H	Me		Me	Et	
721	H	Me		Me	Et	
722	H	Me		Me	Et	
723	H	Me		Me	Et	
724	H	Me		Me	Et	
725	H	Me		Me	Et	
726	H	Me		Me	Et	
727	H	Me		Me	Et	
728	H	Me		Me	Et	

表-1(つづき)


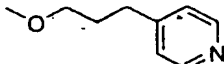

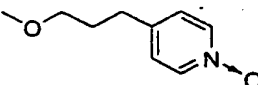

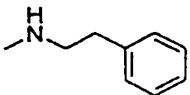

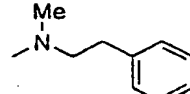

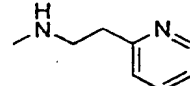

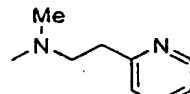

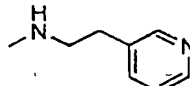

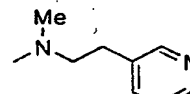

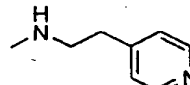

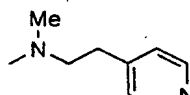

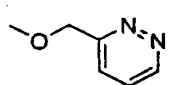

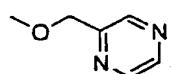

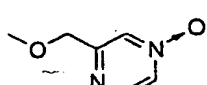

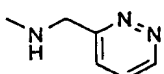

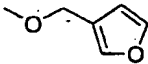

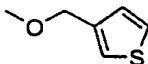

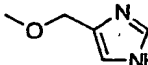

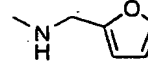

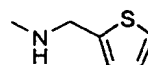

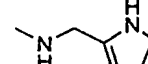

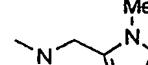

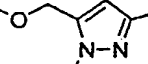






化合物No	X	R1	R2	R3	R4	R5
729	H	Me		Me	Et	
730	H	Me		Me	Et	
731	H	Me		Me	Et	
732	H	Me		Me	Et	
733	H	Me		Me	Et	
734	H	Me		Me	Et	
735	H	Me		Me	Et	
736	H	Me		Me	Et	
737	H	Me		Me	Et	
738	H	Me		Me	Et	
739	H	Me		Me	Et	
740	H	Me		Me	Et	
741	H	Me		Me	Et	
742	H	Me		Me	Et	

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
743	H	Me		Me	Et	
744	H	Me		Me	Et	
745	H	Me		Me	Et	
746	H	Me		Me	Et	
747	H	Me		Me	Et	
748	H	Me		Me	Et	
749	H	Me		Me	Et	
750	H	Me		Me	Et	
751	H	Me		Me	OMe	H
752	H	Me		Me	OMe	OMe
753	H	Me		Me	OMe	F
754	H	Me		Me	OMe	Cl
755	H	Me		Me	OMe	Br
756	H	Me		Me	OMe	I

表一(つづき)


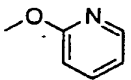

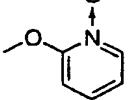

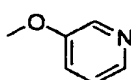

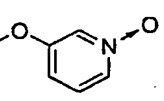

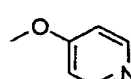

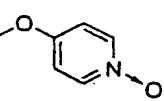

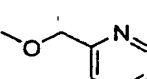

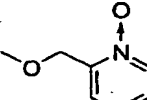

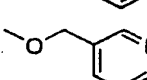

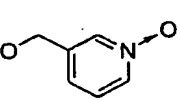

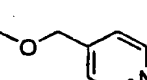

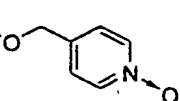

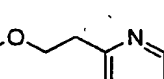

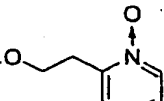
化合物No	X	R1	R2	R3	R4	R5
757	H	Me		Me	OMe	
758	H	Me		Me	OMe	
759	H	Me		Me	OMe	
760	H	Me		Me	OMe	
761	H	Me		Me	OMe	
762	H	Me		Me	OMe	
763	H	Me		Me	OMe	
764	H	Me		Me	OMe	
765	H	Me		Me	OMe	
766	H	Me		Me	OMe	
767	H	Me		Me	OMe	
768	H	Me		Me	OMe	
769	H	Me		Me	OMe	
770	H	Me		Me	OMe	

表-1(つづき)


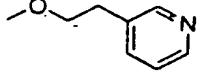

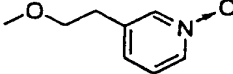

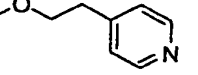

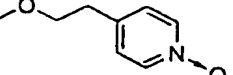

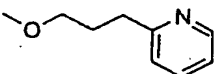

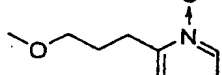

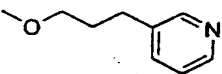

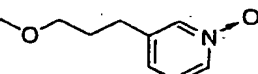

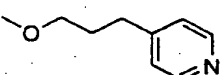

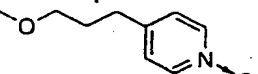

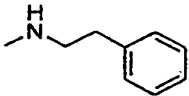

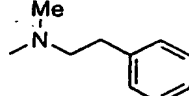

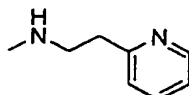

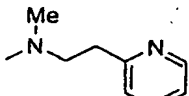
化合物No	X	R1	R2	R3	R4	R5
771	H	Me		Me	OMe	
772	H	Me		Me	OMe	
773	H	Me		Me	OMe	
774	H	Me		Me	OMe	
775	H	Me		Me	OMe	
776	H	Me		Me	OMe	
777	H	Me		Me	OMe	
778	H	Me		Me	OMe	
779	H	Me		Me	OMe	
780	H	Me		Me	OMe	
781	H	Me		Me	OMe	
782	H	Me		Me	OMe	
783	H	Me		Me	OMe	
784	H	Me		Me	OMe	

表-1(つづき)


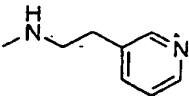

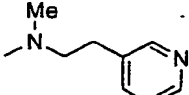

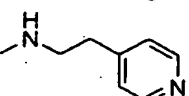

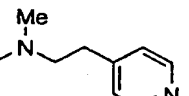

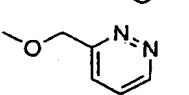

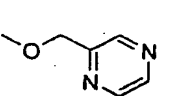

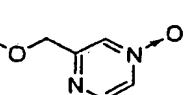

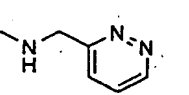

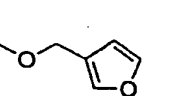

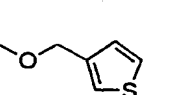

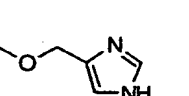

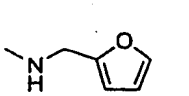

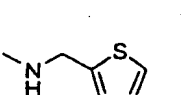

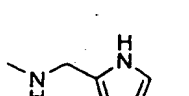
化合物No	X	R1	R2	R3	R4	R5
785	H	Me		Me	OMe	
786	H	Me		Me	OMe	
787	H	Me		Me	OMe	
788	H	Me		Me	OMe	
789	H	Me		Me	OMe	
790	H	Me		Me	OMe	
791	H	Me		Me	OMe	
792	H	Me		Me	OMe	
793	H	Me		Me	OMe	
794	H	Me		Me	OMe	
795	H	Me		Me	OMe	
796	H	Me		Me	OMe	
797	H	Me		Me	OMe	
798	H	Me		Me	OMe	

表-1(つづき)


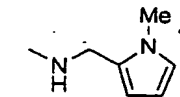

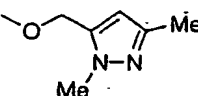







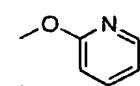

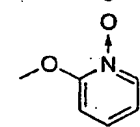

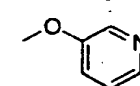

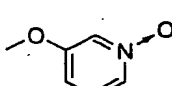

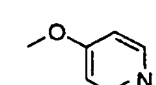

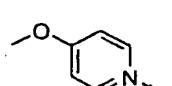
化合物No	X	R1	R2	R3	R4	R5
799	H	Me		Me	OMe	
800	H	Me		Me	OMe	
801	H	Me		Me	NH ₂	H
802	H	Me		Me	NH ₂	OMe
803	H	Me		Me	NH ₂	F
804	H	Me		Me	NH ₂	Cl
805	H	Me		Me	NH ₂	Br
806	H	Me		Me	NH ₂	I
807	H	Me		Me	NH ₂	
808	H	Me		Me	NH ₂	
809	H	Me		Me	NH ₂	
810	H	Me		Me	NH ₂	
811	H	Me		Me	NH ₂	
812	H	Me		Me	NH ₂	

表-1(つづき)


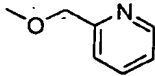

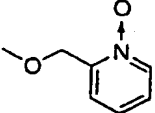

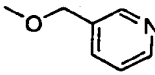

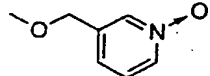

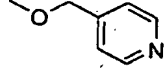

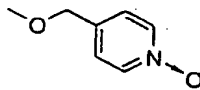

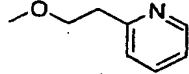

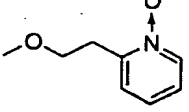

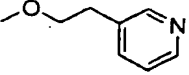

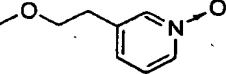

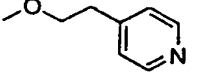

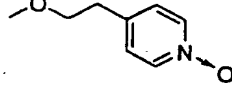

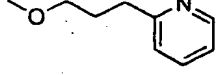

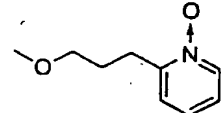
化合物No	X	R1	R2	R3	R4	R5
813	H	Me		Me	NH ₂	
814	H	Me		Me	NH ₂	
815	H	Me		Me	NH ₂	
816	H	Me		Me	NH ₂	
817	H	Me		Me	NH ₂	
818	H	Me		Me	NH ₂	
819	H	Me		Me	NH ₂	
820	H	Me		Me	NH ₂	
821	H	Me		Me	NH ₂	
822	H	Me		Me	NH ₂	
823	H	Me		Me	NH ₂	
824	H	Me		Me	NH ₂	
825	H	Me		Me	NH ₂	
826	H	Me		Me	NH ₂	

表-1(つづき)


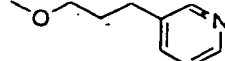

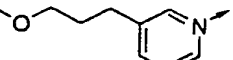

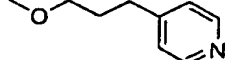

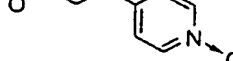

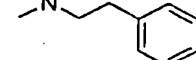

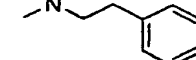



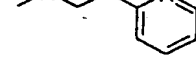







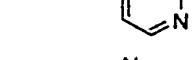




化合物No	X	R1	R2	R3	R4	R5
827	H	Me		Me	NH ₂	
828	H	Me		Me	NH ₂	
829	H	Me		Me	NH ₂	
830	H	Me		Me	NH ₂	
831	H	Me		Me	NH ₂	
832	H	Me		Me	NH ₂	
833	H	Me		Me	NH ₂	
834	H	Me		Me	NH ₂	
835	H	Me		Me	NH ₂	
836	H	Me		Me	NH ₂	
837	H	Me		Me	NH ₂	
838	H	Me		Me	NH ₂	
839	H	Me		Me	NH ₂	
840	H	Me		Me	NH ₂	

表-1(つづき)


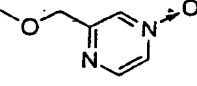

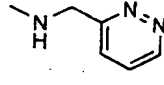

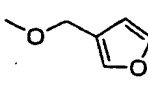

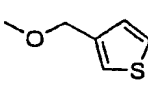

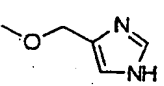

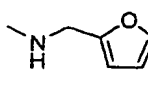

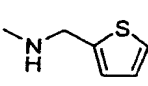

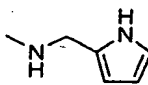

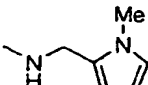

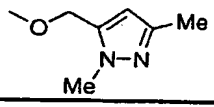




化合物No	X	R1	R2	R3	R4	R5
841	H	Me		Me	NH ₂	
842	H	Me		Me	NH ₂	
843	H	Me		Me	NH ₂	
844	H	Me		Me	NH ₂	
845	H	Me		Me	NH ₂	
846	H	Me		Me	NH ₂	
847	H	Me		Me	NH ₂	
848	H	Me		Me	NH ₂	
849	H	Me		Me	NH ₂	
850	H	Me		Me	NH ₂	
851	H	Me		Me	NHMe	H
852	H	Me		Me	NHMe	OMe
853	H	Me		Me	NHMe	F
854	H	Me		Me	NHMe	Cl

表-1(つづき)




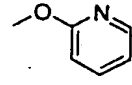

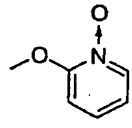

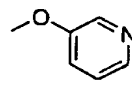

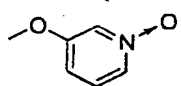

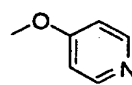

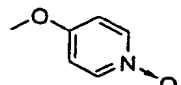

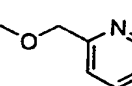

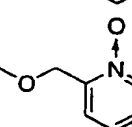

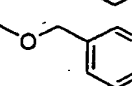

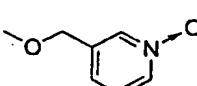

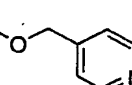

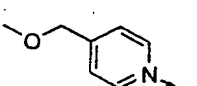
化合物No	X	R1	R2	R3	R4	R5
855	H	Me		Me	NHMe	Br
856	H	Me		Me	NHMe	I
857	H	Me		Me	NHMe	
858	H	Me		Me	NHMe	
859	H	Me		Me	NHMe	
860	H	Me		Me	NHMe	
861	H	Me		Me	NHMe	
862	H	Me		Me	NHMe	
863	H	Me		Me	NHMe	
864	H	Me		Me	NHMe	
865	H	Me		Me	NHMe	
866	H	Me		Me	NHMe	
867	H	Me		Me	NHMe	
868	H	Me		Me	NHMe	

表-1(つづき)


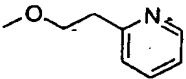

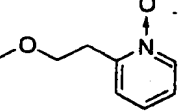

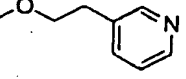

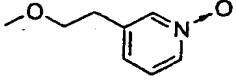

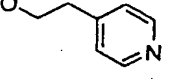

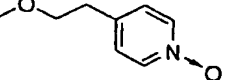

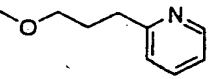

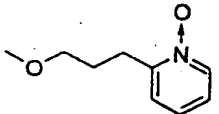

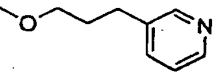

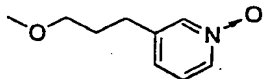

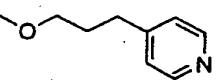

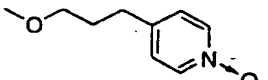

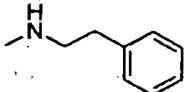

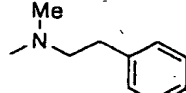
化合物No	X	R1	R2	R3	R4	R5
869	H	Me		Me	NHMe	
870	H	Me		Me	NHMe	
871	H	Me		Me	NHMe	
872	H	Me		Me	NHMe	
873	H	Me		Me	NHMe	
874	H	Me		Me	NHMe	
875	H	Me		Me	NHMe	
876	H	Me		Me	NHMe	
877	H	Me		Me	NHMe	
878	H	Me		Me	NHMe	
879	H	Me		Me	NHMe	
880	H	Me		Me	NHMe	
881	H	Me		Me	NHMe	
882	H	Me		Me	NHMe	

表-1(つづき)


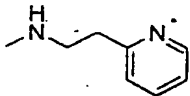

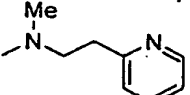

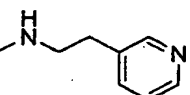

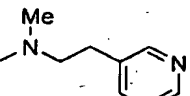

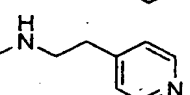

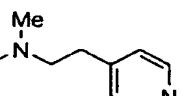

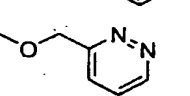

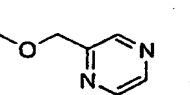

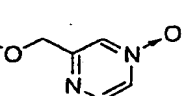

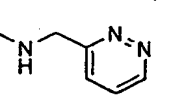

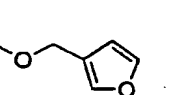

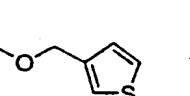

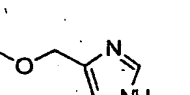

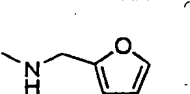
化合物No	X	R1	R2	R3	R4	R5
883	H	Me		Me	NHMe	
884	H	Me		Me	NHMe	
885	H	Me		Me	NHMe	
886	H	Me		Me	NHMe	
887	H	Me		Me	NHMe	
888	H	Me		Me	NHMe	
889	H	Me		Me	NHMe	
890	H	Me		Me	NHMe	
891	H	Me		Me	NHMe	
892	H	Me		Me	NHMe	
893	H	Me		Me	NHMe	
894	H	Me		Me	NHMe	
895	H	Me		Me	NHMe	
896	H	Me		Me	NHMe	

表-1(つづき)


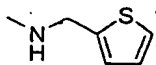

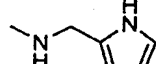

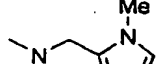

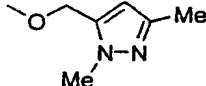







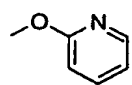

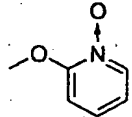

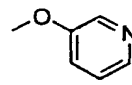

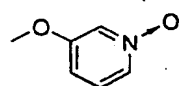
化合物No	X	R1	R2	R3	R4	R5
897	H	Me		Me	NHMe	
898	H	Me		Me	NHMe	
899	H	Me		Me	NHMe	
900	H	Me		Me	NHMe	
901	H	Me		Me	NHEt	H
902	H	Me		Me	NHEt	OMe
903	H	Me		Me	NHEt	F
904	H	Me		Me	NHEt	Cl
905	H	Me		Me	NHEt	Br
906	H	Me		Me	NHEt	I
907	H	Me		Me	NHEt	
908	H	Me		Me	NHEt	
909	H	Me		Me	NHEt	
910	H	Me		Me	NHEt	

表-1(つづき)


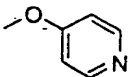

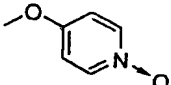

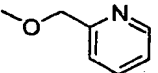

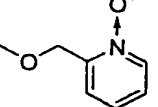

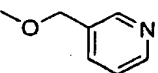

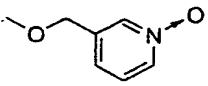

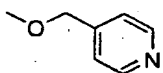

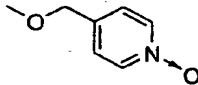

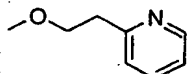

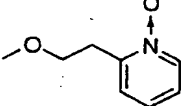

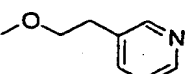

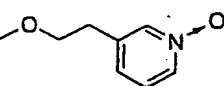

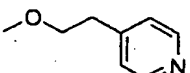

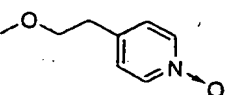
化合物No	X	R1	R2	R3	R4	R5
911	H	Me		Me	NHEt	
912	H	Me		Me	NHEt	
913	H	Me		Me	NHEt	
914	H	Me		Me	NHEt	
915	H	Me		Me	NHEt	
916	H	Me		Me	NHEt	
917	H	Me		Me	NHEt	
918	H	Me		Me	NHEt	
919	H	Me		Me	NHEt	
920	H	Me		Me	NHEt	
921	H	Me		Me	NHEt	
922	H	Me		Me	NHEt	
923	H	Me		Me	NHEt	
924	H	Me		Me	NHEt	

表-1(つづき)


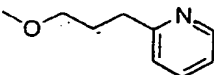

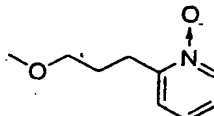

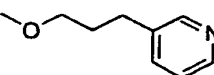

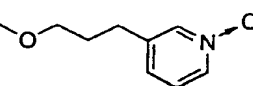

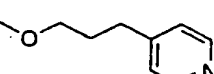

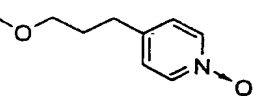

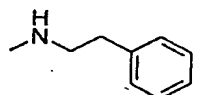

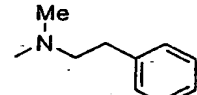

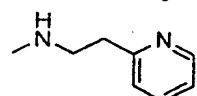

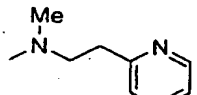

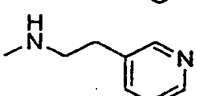

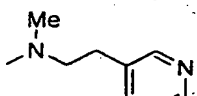

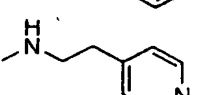

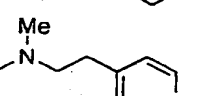
化合物No	X	R1	R2	R3	R4	R5
925	H	Me		Me	NHEt	
926	H	Me		Me	NHEt	
927	H	Me		Me	NHEt	
928	H	Me		Me	NHEt	
929	H	Me		Me	NHEt	
930	H	Me		Me	NHEt	
931	H	Me		Me	NHEt	
932	H	Me		Me	NHEt	
933	H	Me		Me	NHEt	
934	H	Me		Me	NHEt	
935	H	Me		Me	NHEt	
936	H	Me		Me	NHEt	
937	H	Me		Me	NHEt	
938	H	Me		Me	NHEt	

表-1(つづき)


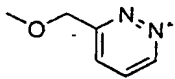

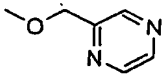

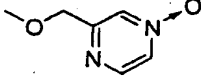

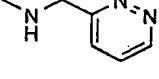

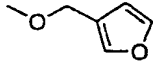

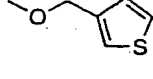

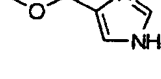

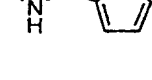

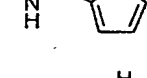

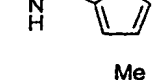

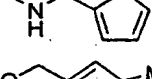

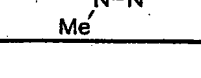


化合物No	X	R1	R2	R3	R4	R5
939	H	Me		Me	NHEt	
940	H	Me		Me	NHEt	
941	H	Me		Me	NHEt	
942	H	Me		Me	NHEt	
943	H	Me		Me	NHEt	
944	H	Me		Me	NHEt	
945	H	Me		Me	NHEt	
946	H	Me		Me	NHEt	
947	H	Me		Me	NHEt	
948	H	Me		Me	NHEt	
949	H	Me		Me	NHEt	
950	H	Me		Me	NHEt	
951	H	Me		Me	NH <i>n</i> -Pr	H
952	H	Me		Me	NH <i>n</i> -Pr	OMe

表-1(つづき)






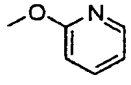

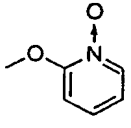

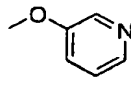

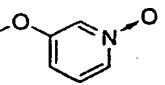

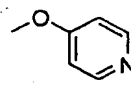

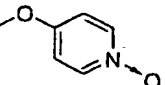

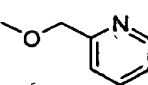

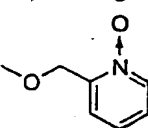

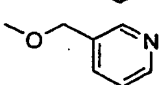

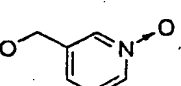
化合物No	X	R1	R2	R3	R4	R5
953	H	Me		Me	NH <i>n</i> -Pr	F
954	H	Me		Me	NH <i>n</i> -Pr	Cl
955	H	Me		Me	NH <i>n</i> -Pr	Br
956	H	Me		Me	NH <i>n</i> -Pr	I
957	H	Me		Me	NH <i>n</i> -Pr	
958	H	Me		Me	NH <i>n</i> -Pr	
959	H	Me		Me	NH <i>n</i> -Pr	
960	H	Me		Me	NH <i>n</i> -Pr	
961	H	Me		Me	NH <i>n</i> -Pr	
962	H	Me		Me	NH <i>n</i> -Pr	
963	H	Me		Me	NH <i>n</i> -Pr	
964	H	Me		Me	NH <i>n</i> -Pr	
965	H	Me		Me	NH <i>n</i> -Pr	
966	H	Me		Me	NH <i>n</i> -Pr	

表-1(つづき)


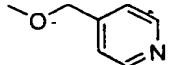

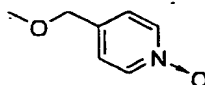

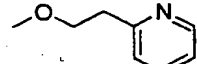

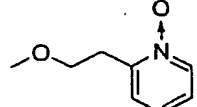

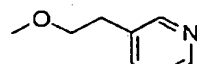

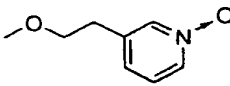

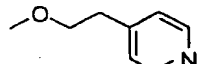

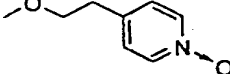

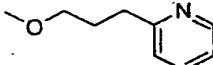

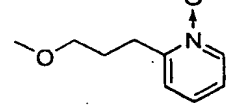

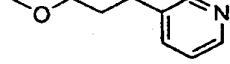

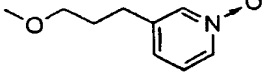

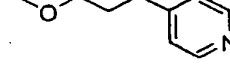

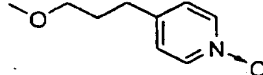
化合物No	X	R1	R2	R3	R4	R5
967	H	Me		Me	NH <i>n</i> -Pr	
968	H	Me		Me	NH <i>n</i> -Pr	
969	H	Me		Me	NH <i>n</i> -Pr	
970	H	Me		Me	NH <i>n</i> -Pr	
971	H	Me		Me	NH <i>n</i> -Pr	
972	H	Me		Me	NH <i>n</i> -Pr	
973	H	Me		Me	NH <i>n</i> -Pr	
974	H	Me		Me	NH <i>n</i> -Pr	
975	H	Me		Me	NH <i>n</i> -Pr	
976	H	Me		Me	NH <i>n</i> -Pr	
977	H	Me		Me	NH <i>n</i> -Pr	
978	H	Me		Me	NH <i>n</i> -Pr	
979	H	Me		Me	NH <i>n</i> -Pr	
980	H	Me		Me	NH <i>n</i> -Pr	

表-1(つづき)


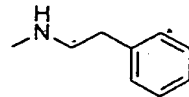

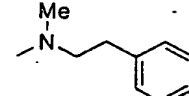

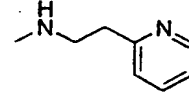

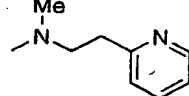

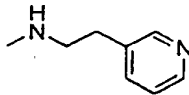

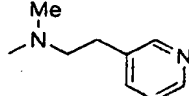

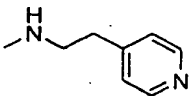

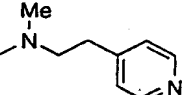

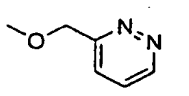

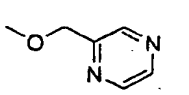

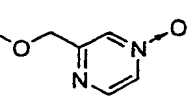

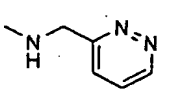

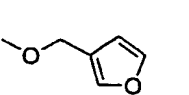

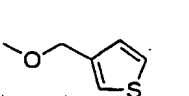
化合物No	X	R1	R2	R3	R4	R5
981	H	Me		Me	NH <i>n</i> -Pr	
982	H	Me		Me	NH <i>n</i> -Pr	
983	H	Me		Me	NH <i>n</i> -Pr	
984	H	Me		Me	NH <i>n</i> -Pr	
985	H	Me		Me	NH <i>n</i> -Pr	
986	H	Me		Me	NH <i>n</i> -Pr	
987	H	Me		Me	NH <i>n</i> -Pr	
988	H	Me		Me	NH <i>n</i> -Pr	
989	H	Me		Me	NH <i>n</i> -Pr	
990	H	Me		Me	NH <i>n</i> -Pr	
991	H	Me		Me	NH <i>n</i> -Pr	
992	H	Me		Me	NH <i>n</i> -Pr	
993	H	Me		Me	NH <i>n</i> -Pr	
994	H	Me		Me	NH <i>n</i> -Pr	

表-1(つづき)


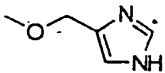

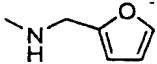

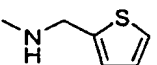

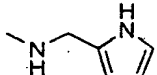

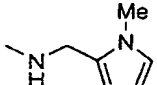

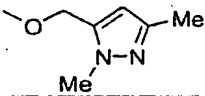







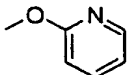

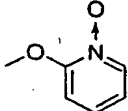

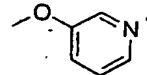

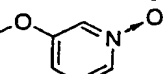

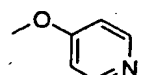

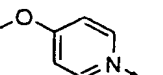

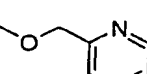

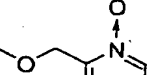

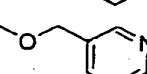

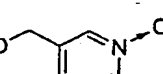

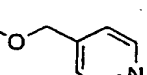

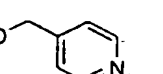

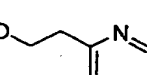

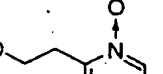

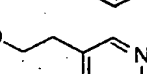

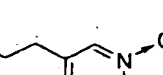

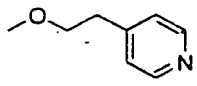

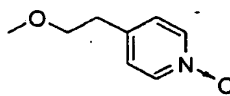

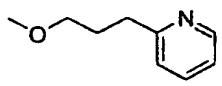

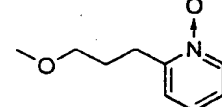

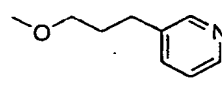

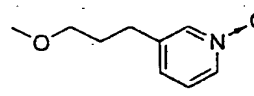

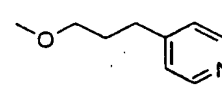

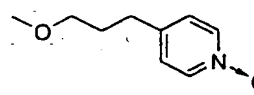

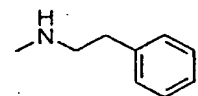

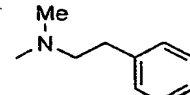

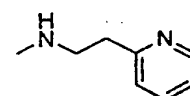

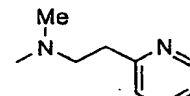

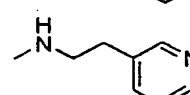

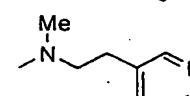
化合物No	X	R1	R2	R3	R4	R5
995	H	Me		Me	NH <i>n</i> -Pr	
996	H	Me		Me	NH <i>n</i> -Pr	
997	H	Me		Me	NH <i>n</i> -Pr	
998	H	Me		Me	NH <i>n</i> -Pr	
999	H	Me		Me	NH <i>n</i> -Pr	
1000	H	Me		Me	NH <i>n</i> -Pr	
1001	H	Me		Me	NMe ₂	H
1002	H	Me		Me	NMe ₂	OMe
1003	H	Me		Me	NMe ₂	F
1004	H	Me		Me	NMe ₂	Cl
1005	H	Me		Me	NMe ₂	Br
1006	H	Me		Me	NMe ₂	I
1007	H	Me		Me	NMe ₂	
1008	H	Me		Me	NMe ₂	


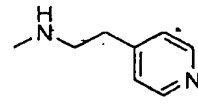

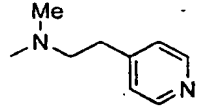

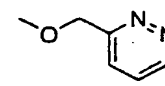

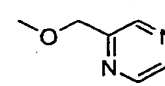

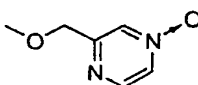

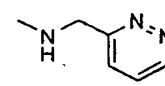

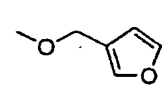

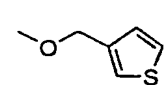

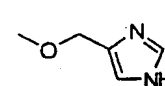

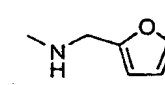

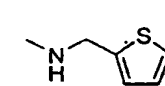

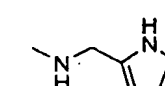

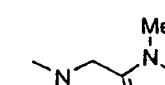

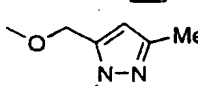
表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
1009	H	Me		Me	NMe ₂	
1010	H	Me		Me	NMe ₂	
1011	H	Me		Me	NMe ₂	
1012	H	Me		Me	NMe ₂	
1013	H	Me		Me	NMe ₂	
1014	H	Me		Me	NMe ₂	
1015	H	Me		Me	NMe ₂	
1016	H	Me		Me	NMe ₂	
1017	H	Me		Me	NMe ₂	
1018	H	Me		Me	NMe ₂	
1019	H	Me		Me	NMe ₂	
1020	H	Me		Me	NMe ₂	
1021	H	Me		Me	NMe ₂	
1022	H	Me		Me	NMe ₂	

表一(つづき)

化合物No	X	R1	R2	R3	R4	R5
1023	H	Me		Me	NMe ₂	
1024	H	Me		Me	NMe ₂	
1025	H	Me		Me	NMe ₂	
1026	H	Me		Me	NMe ₂	
1027	H	Me		Me	NMe ₂	
1028	H	Me		Me	NMe ₂	
1029	H	Me		Me	NMe ₂	
1030	H	Me		Me	NMe ₂	
1031	H	Me		Me	NMe ₂	
1032	H	Me		Me	NMe ₂	
1033	H	Me		Me	NMe ₂	
1034	H	Me		Me	NMe ₂	
1035	H	Me		Me	NMe ₂	
1036	H	Me		Me	NMe ₂	

表一(つづき)

化合物No	X	R1	R2	R3	R4	R5
1037	H	Me		Me	NMe ₂	
1038	H	Me		Me	NMe ₂	
1039	H	Me		Me	NMe ₂	
1040	H	Me		Me	NMe ₂	
1041	H	Me		Me	NMe ₂	
1042	H	Me		Me	NMe ₂	
1043	H	Me		Me	NMe ₂	
1044	H	Me		Me	NMe ₂	
1045	H	Me		Me	NMe ₂	
1046	H	Me		Me	NMe ₂	
1047	H	Me		Me	NMe ₂	
1048	H	Me		Me	NMe ₂	
1049	H	Me		Me	NMe ₂	
1050	H	Me		Me	NMe ₂	

表一(つづき)








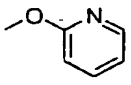

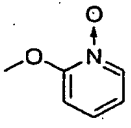

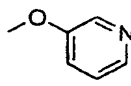

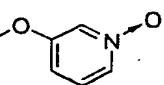

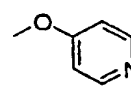

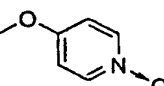

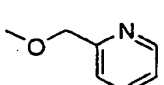

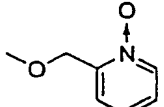
化合物No	X	R1	R2	R3	R4	R5
1051	H	Me		Me	Cl	H
1052	H	Me		Me	Cl	OMe
1053	H	Me		Me	Cl	F
1054	H	Me		Me	Cl	Cl
1055	H	Me		Me	Cl	Br
1056	H	Me		Me	Cl	I
1057	H	Me		Me	Cl	
1058	H	Me		Me	Cl	
1059	H	Me		Me	Cl	
1060	H	Me		Me	Cl	
1061	H	Me		Me	Cl	
1062	H	Me		Me	Cl	
1063	H	Me		Me	Cl	
1064	H	Me		Me	Cl	

表-1(つづき)


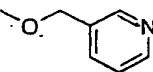

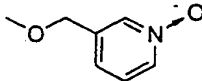

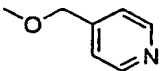

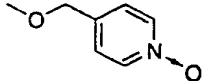

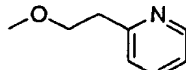

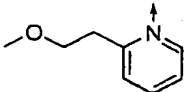

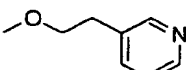

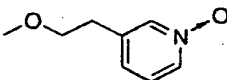

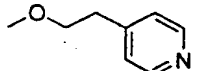

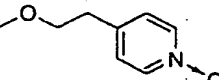

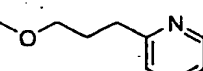

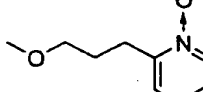

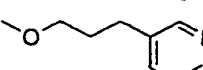

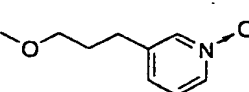

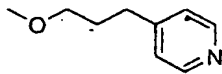

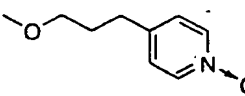

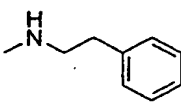

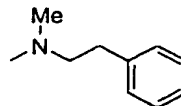

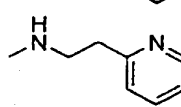

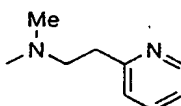

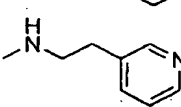

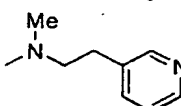

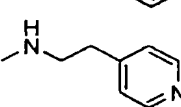

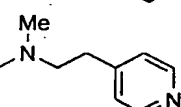

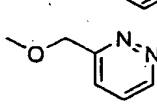

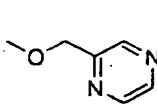

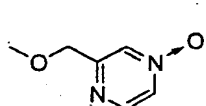

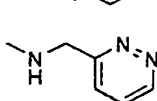
化合物No	X	R1	R2	R3	R4	R5
1065	H	Me		Me	Cl	
1066	H	Me		Me	Cl	
1067	H	Me		Me	Cl	
1068	H	Me		Me	Cl	
1069	H	Me		Me	Cl	
1070	H	Me		Me	Cl	
1071	H	Me		Me	Cl	
1072	H	Me		Me	Cl	
1073	H	Me		Me	Cl	
1074	H	Me		Me	Cl	
1075	H	Me		Me	Cl	
1076	H	Me		Me	Cl	
1077	H	Me		Me	Cl	
1078	H	Me		Me	Cl	

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
1079	H	Me		Me	Cl	
1080	H	Me		Me	Cl	
1081	H	Me		Me	Cl	
1082	H	Me		Me	Cl	
1083	H	Me		Me	Cl	
1084	H	Me		Me	Cl	
1085	H	Me		Me	Cl	
1086	H	Me		Me	Cl	
1087	H	Me		Me	Cl	
1088	H	Me		Me	Cl	
1089	H	Me		Me	Cl	
1090	H	Me		Me	Cl	
1091	H	Me		Me	Cl	
1092	H	Me		Me	Cl	

表一1(つづき)


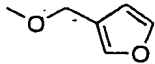

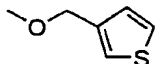

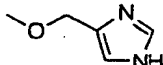

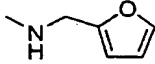

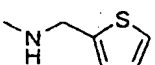

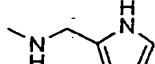

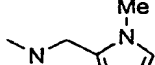

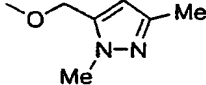












化合物No	X	R1	R2	R3	R4	R5
1093	H	Me		Me	Cl	
1094	H	Me		Me	Cl	
1095	H	Me		Me	Cl	
1096	H	Me		Me	Cl	
1097	H	Me		Me	Cl	
1098	H	Me		Me	Cl	
1099	H	Me		Me	Cl	
1100	H	Me		Me	Cl	
1101	H	Me		Me		H
1102	H	Me		Me		OMe
1103	H	Me		Me		F
1104	H	Me		Me		Cl
1105	H	Me		Me		Br
1106	H	Me		Me		I

表-1(つづき)



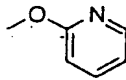


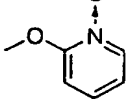


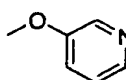


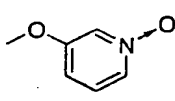


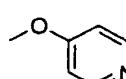


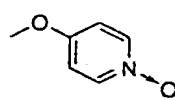


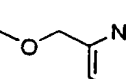


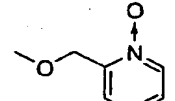


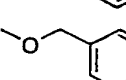


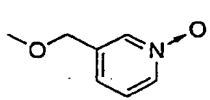


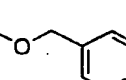


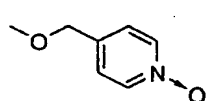


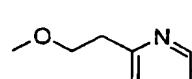


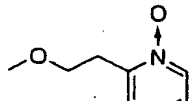
化合物No	X	R1	R2	R3	R4	R5
1107	H	Me		Me		
1108	H	Me		Me		
1109	H	Me		Me		
1110	H	Me		Me		
1111	H	Me		Me		
1112	H	Me		Me		
1113	H	Me		Me		
1114	H	Me		Me		
1115	H	Me		Me		
1116	H	Me		Me		
1117	H	Me		Me		
1118	H	Me		Me		
1119	H	Me		Me		
1120	H	Me		Me		

表-1(つづき)



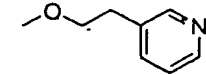


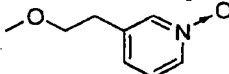


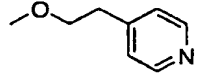


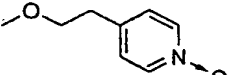


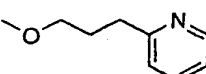


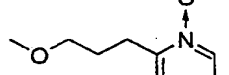


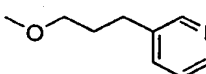


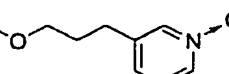


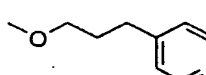


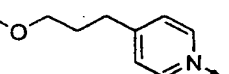


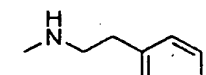


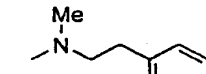


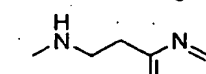


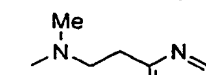
化合物No	X	R1	R2	R3	R4	R5
1121	H	Me		Me		
1122	H	Me		Me		
1123	H	Me		Me		
1124	H	Me		Me		
1125	H	Me		Me		
1126	H	Me		Me		
1127	H	Me		Me		
1128	H	Me		Me		
1129	H	Me		Me		
1130	H	Me		Me		
1131	H	Me		Me		
1132	H	Me		Me		
1133	H	Me		Me		
1134	H	Me		Me		

表-1(つづき)



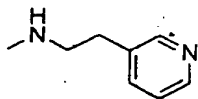


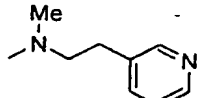


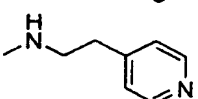


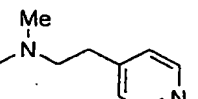


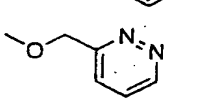


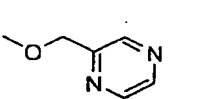


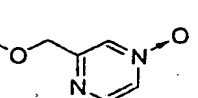


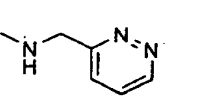


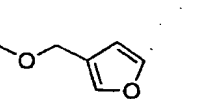


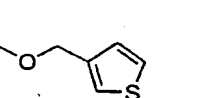


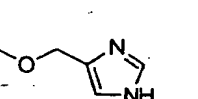


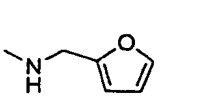


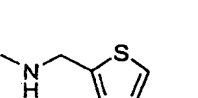


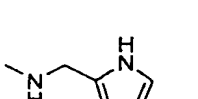
化合物No	X	R1	R2	R3	R4	R5
1135	H	Me		Me		
1136	H	Me		Me		
1137	H	Me		Me		
1138	H	Me		Me		
1139	H	Me		Me		
1140	H	Me		Me		
1141	H	Me		Me		
1142	H	Me		Me		
1143	H	Me		Me		
1144	H	Me		Me		
1145	H	Me		Me		
1146	H	Me		Me		
1147	H	Me		Me		
1148	H	Me		Me		

表-1(つづき)



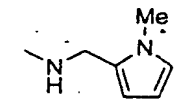


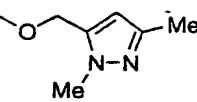

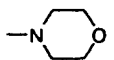

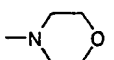

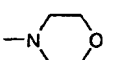

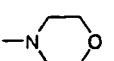

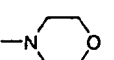

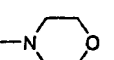

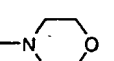
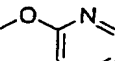

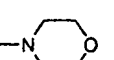
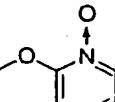

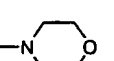
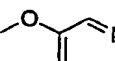

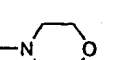
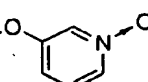

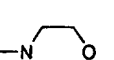
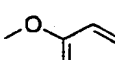

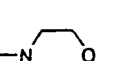
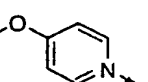
化合物No	X	R1	R2	R3	R4	R5
1149	H	Me		Me		
1150	H	Me		Me		
1151	H	Me		Me		H
1152	H	Me		Me		OMe
1153	H	Me		Me		F
1154	H	Me		Me		Cl
1155	H	Me		Me		Br
1156	H	Me		Me		I
1157	H	Me		Me		
1158	H	Me		Me		
1159	H	Me		Me		
1160	H	Me		Me		
1161	H	Me		Me		
1162	H	Me		Me		

表-1(つづき)


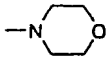
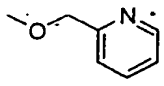

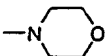
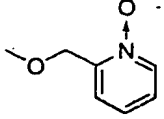

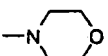
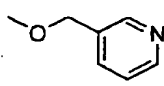

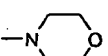
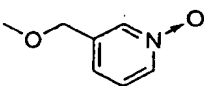

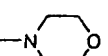
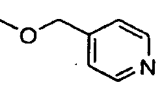

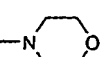
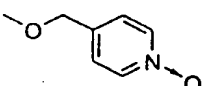

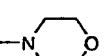
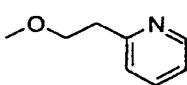

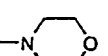
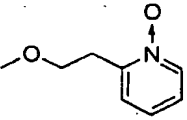

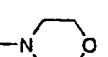
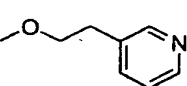

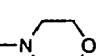
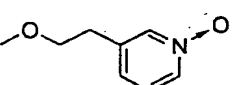

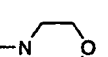
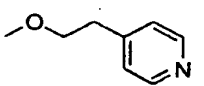

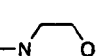
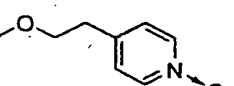

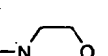
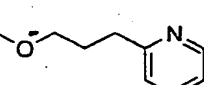

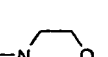
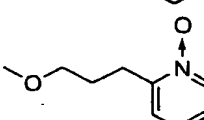
化合物No	X	R1	R2	R3	R4	R5
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1164	H	Me		Me		
1165	H	Me		Me		
1166	H	Me		Me		
1167	H	Me		Me		
1168	H	Me		Me		
1169	H	Me		Me		
1170	H	Me		Me		
1171	H	Me		Me		
1172	H	Me		Me		
1173	H	Me		Me		
1174	H	Me		Me		
1175	H	Me		Me		
1176	H	Me		Me		

表-1(つづき)


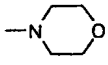
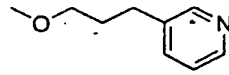

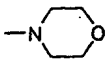
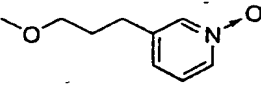

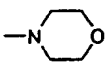
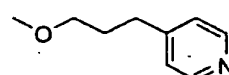

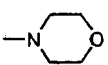
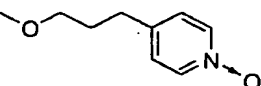

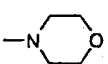
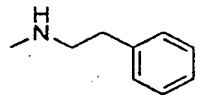

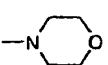
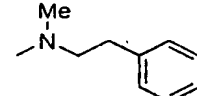

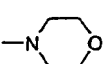
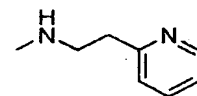

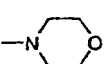
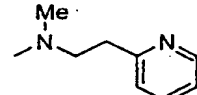

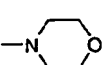
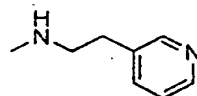

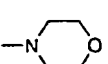
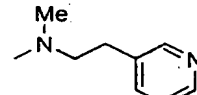

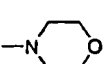
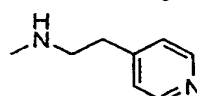

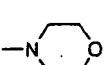
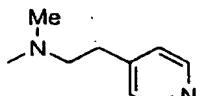

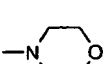
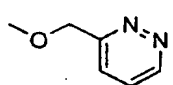

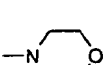
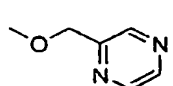

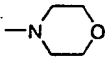
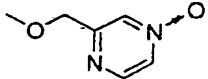

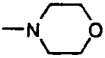
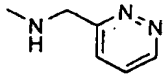

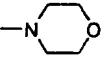
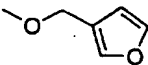

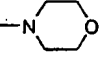
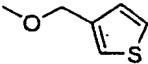

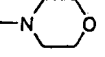
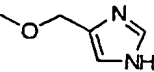

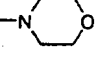
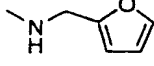

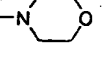
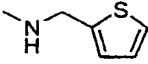

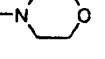
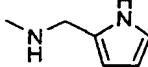

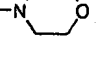
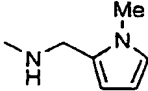

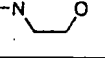
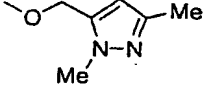
化合物No	X	R1	R2	R3	R4	R5
1177	H	Me		Me		
1178	H	Me		Me		
1179	H	Me		Me		
1180	H	Me		Me		
1181	H	Me		Me		
1182	H	Me		Me		
1183	H	Me		Me		
1184	H	Me		Me		
1185	H	Me		Me		
1186	H	Me		Me		
1187	H	Me		Me		
1188	H	Me		Me		
1189	H	Me		Me		
1190	H	Me		Me		

表-1(つづき)

化合物No	X	R1	R2	R3	R4	R5
1191	H	Me		Me		
1192	H	Me		Me		
1193	H	Me		Me		
1194	H	Me		Me		
1195	H	Me		Me		
1196	H	Me		Me		
1197	H	Me		Me		
1198	H	Me		Me		
1199	H	Me		Me		
1200	H	Me		Me		

本発明の化合物の特に好ましい例として、以下の化合物が挙げられるが、本発明の化合物はこれらに限定されることはない。

- 2-クロロ-9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン;
- 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-メトキシプリン;
- 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-(ピリダジニルメチルオキシ)プリン;
- 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[4-ピリジルメチルオキシ]プリン;
- 4-[[9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン]-2-イル-オキシメチル]ピリジン N-オキシド;
- 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[2-(4-ピリジル)エチルオキシ]プリン;
- 4-[[9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン]-2-イル-2-オキシエチル]ピリジン N-オキシド;
- 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6-メチルアミノ-2-(3-ピリダニルメチルオキシ)プリン;
- 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[2-(4-ピリジル)エチルアミノ]プリン;
- 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[(4-ピリジル)メチルアミノ]プリン;
- 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[3-(4-ピリジル)プロピルオキシ]プリン;及び
- 4-[[9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン]-2-イル-3-オキシプロピル]ピリジン N-オキシド.

上記一般式(I)で表される化合物の塩類としては、生理的に許容される塩類

が好ましく、例えば、塩酸塩、臭化水素酸塩、ヨウ化水素酸塩、硫酸塩、リン酸塩等の無機酸塩、及びシュウ酸塩、マレイン酸塩、フマル酸塩、乳酸塩、リンゴ酸塩、クエン酸塩、酒石酸塩、安息香酸塩、メタンスルホン酸塩、p-トルエンスルホン酸塩等の有機酸塩が挙げられる。式(I)の化合物、N-オキシド誘導体、又はその塩は水和物又は溶媒和物の形で存在する場合もあるが、これらの水和物及び溶媒和物も本発明の範囲に包含される。溶媒和物を形成する溶媒としては、例えば、メタノール、エタノール、イソプロパノール、アセトン、酢酸エチル、又は塩化メチレンなどが挙げられる。

なお、本発明のうち、 R^2 がテトラヒドロフラニル基又はビシクロ[2, 2, 1]ヘプト-2-イル基を表す場合は光学対掌体が存在する。また、置換基の種類によっては、1個又は2個以上の不斉炭素を有する場合があります、不斉炭素に基づく光学対掌体又はジアステレオ異性体などの立体異性体が存在する場合がある。純粋な形態の立体異性体、それらの混合物、ラセミ体などはいずれも本発明の範囲に包含される。

本発明により、上記一般式(A)及び(B)で表される化合物が提供されるが、これらの化合物は式(I)で表される前記プリン誘導体の製造用中間体として有用である。一般式(A)及び(B)で表される化合物において、 R^1 、 R^2 、及び R^4 は、前記一般式(I)の化合物について説明した R^1 、 R^2 、及び R^4 と同義である。 R^1 は好ましくは $C_1 \sim C_4$ のアルキル基であり、さらに好ましくは $C_1 \sim C_3$ のアルキル基であり、さらに好ましくはメチル基、エチル基であり、特に好ましくはメチル基である。 R^2 は好ましくはテトラヒドロフラニル基、 $C_1 \sim C_6$ のアルキル基、 $C_1 \sim C_3$ のハロアルキル基、又は $C_3 \sim C_8$ のシクロアルキル基であり、より好ましくは $C_3 \sim C_8$ のシクロアルキル基、さらに好ましくは $C_4 \sim C_6$ のシクロアルキル基であり、特に好ましくはシクロペンチル基である。 R^4 は好ましくは水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基であり、さらに好ましくは $C_1 \sim C_3$ のアルキル基、 $C_1 \sim C_3$ のアルコキシ

基、又は $C_1 \sim C_3$ のアルキルアミノ基である。 X^2 はハロゲン原子を表すが、好ましくは塩素原子である。

一般式(A)で表される化合物の特に好ましい例として、以下の化合物が挙げられる。

4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-2-フルオロ-5-ニトロ-6-メチルピリミジン；

2-クロロ-4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-5-ニトロ-6-メチルピリミジン；

2-ブロモ-4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-5-ニトロ-6-メチルピリミジン；及び

4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-2-イオジド-5-ニトロ-6-メチルピリミジン。

一般式(B)で表される化合物の特に好ましい例として、以下の化合物が挙げられる。

5-アミノ-4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-2-フルオロ-6-メチルピリミジン；

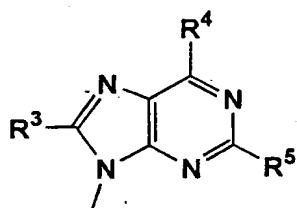
5-アミノ-2-クロロ-4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-6-メチルピリミジン；

5-アミノ-2-ブロモ-4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-6-メチルピリミジン；及び

5-アミノ-4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-2-イオジド-6-メチルピリミジン。

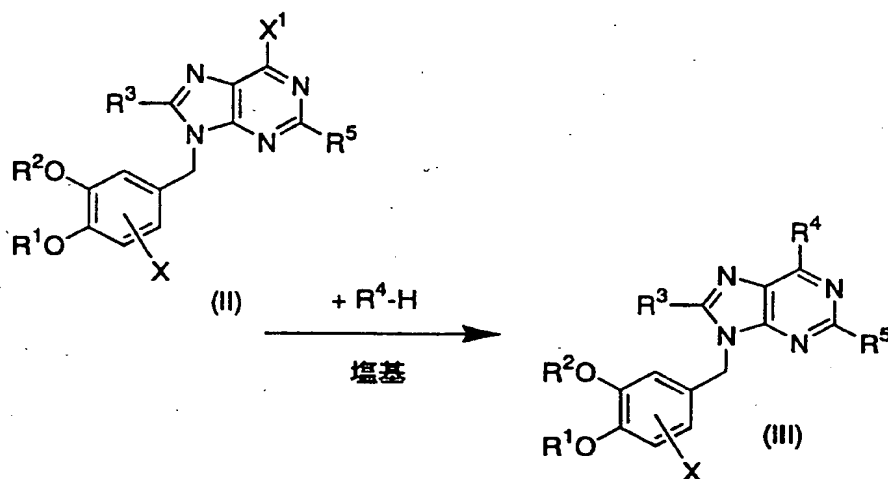
本発明の化合物の製造方法は特に限定されないが、例えば、以下の方法により製造することができる。

Aが下記の式：



で表される基である場合、下記一般式 (III) の化合物は以下の製造方法 1 又は 2 の方法により製造することができる。

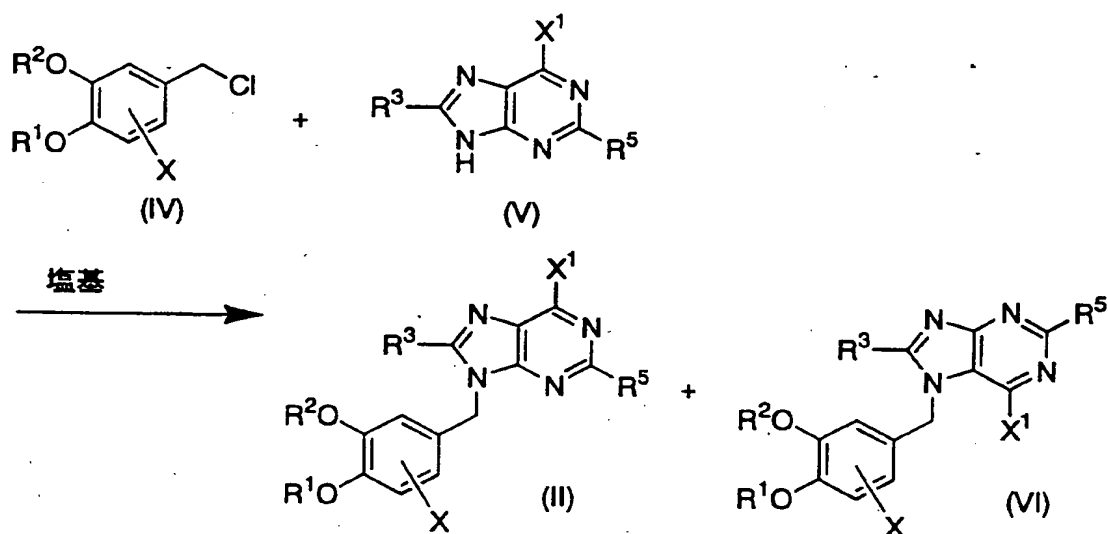
<製造方法 1>



(スキーム中、 R^1 , R^2 , R^3 , R^4 , R^5 、及び X は既に定義したとおりであり、 X^1 はハロゲン原子を表す。)

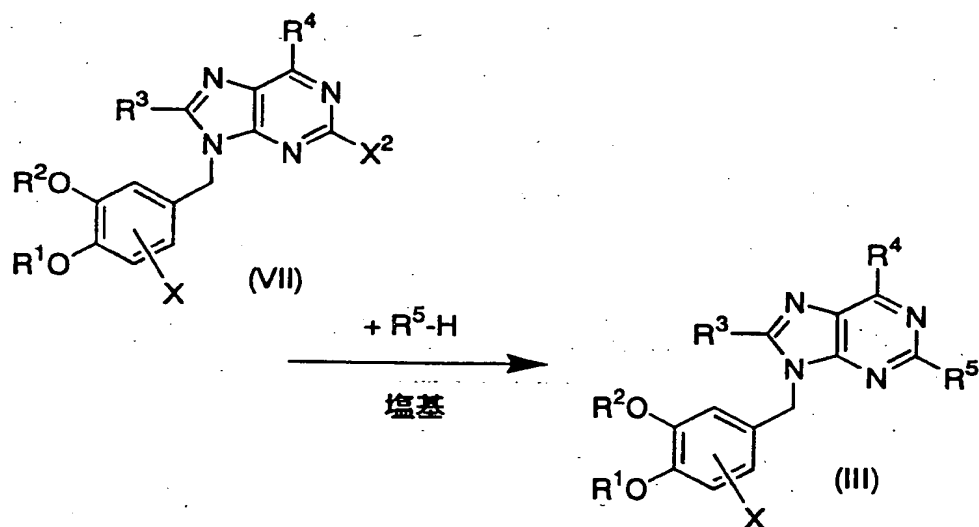
上記反応は、無溶媒又は N, N-ジメチルホルムアミド又はテトラヒドロフラン等の適当な溶媒中、トリエチルアミン、ピリジン、N, N-ジエチルアニリン等の有機塩基、又は炭酸ナトリウム、水素化ナトリウム等の無機塩基の存在下、又は非存在下 0 ~ 150℃ の範囲で行なわれる。

また、上記反応の原料である上記一般式 (II) の化合物は、以下のスキームに従って製造することができる。



(スキーム中、 R^1 , R^2 , R^3 , R^4 , R^5 , X , 及び X^1 は既に定義したとおりである。)

<製造方法2>

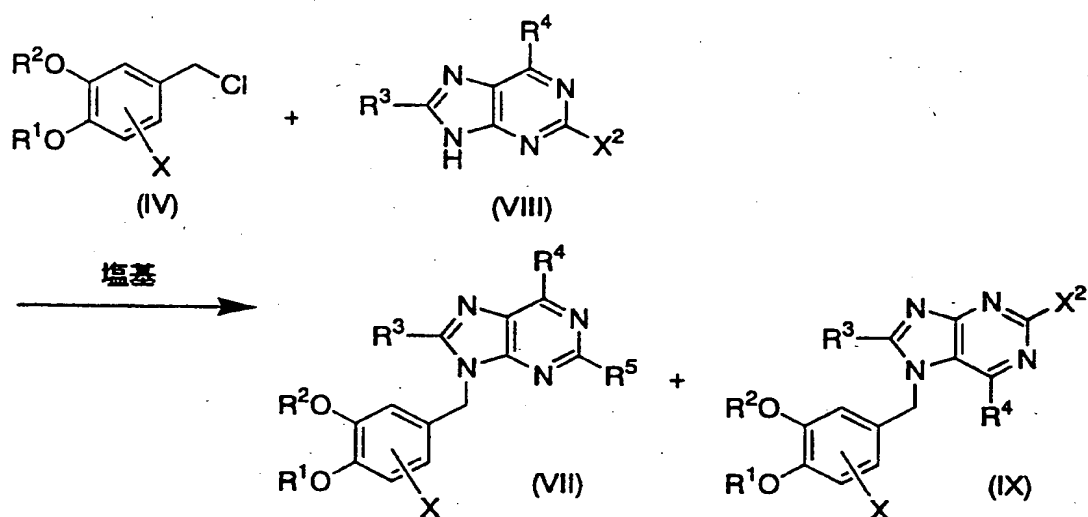


(スキーム中、 R^1 , R^2 , R^3 , R^4 , R^5 , 及び X は既に定義したとおりであり、 X^2 はハロゲン原子を表す。)

上記反応に従って化合物 (VII) と化合物 R^5-H とを縮合することにより、

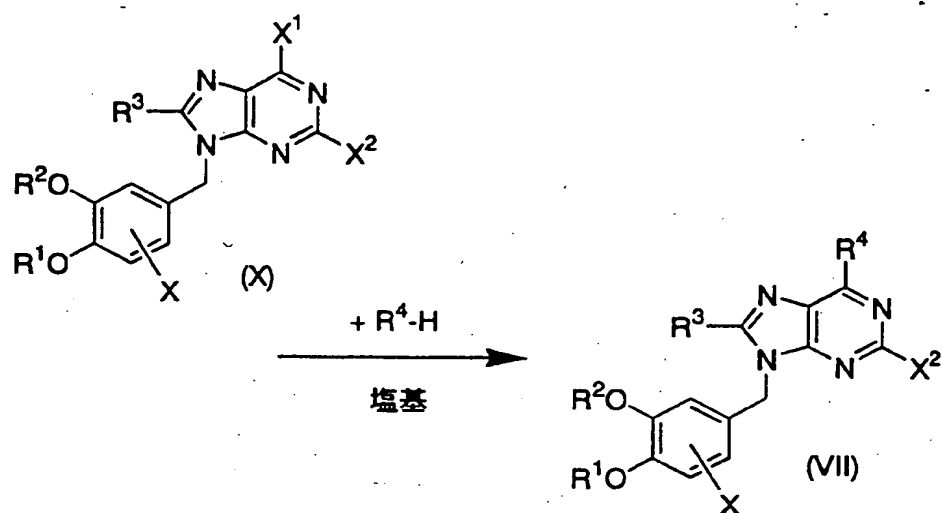
化合物 (III) を調製することができる。N, N-ジメチルホルムアミド又はテトラヒドロフラン等の適当な溶媒、あるいはこれら溶媒を組み合わせた混合溶媒に化合物 R^5-H を加えた後、1 等量～5 等量のトリエチルアミンあるいはピリジン、N, N-ジエチルアニリン等の有機塩基、又は炭酸ナトリウム、水素化ナトリウム等の無機塩基を加えた後、化合物 (VII) を反応させ、目的の化合物 (III) を得ることができる。この反応は、通常、窒素あるいはアルゴン気流下、 $-20 \sim 150^\circ\text{C}$ の範囲で行なわれる。また、上記反応の原料である上記一般式 (VII) の化合物は以下の 3 つの方法で製造することができる。

製造方法①



(スキーム中、 R^1 , R^2 , R^3 , R^4 , R^5 , X , 及び X^2 は既に定義したとおりである。)

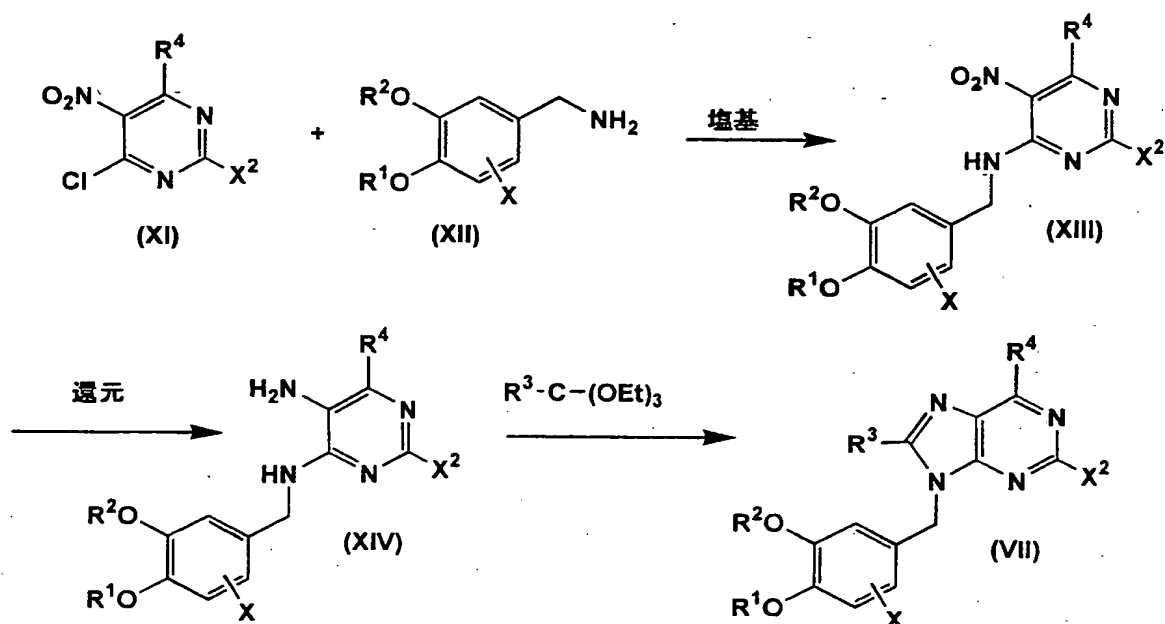
製造方法②



(スキーム中、 R^1 , R^2 , R^3 , R^4 , R^5 , X , X^1 , 及び X^2 は既に定義したとおりである。)

製造方法③

X^2 がハロゲン原子の場合には、一般式 (VII) の化合物は以下の反応式に従って製造することもできる。



(スキーム中、 R^1 , R^2 , R^3 , R^4 , R^5 、及び X は既に定義したとおりであり、 X^2 はハロゲン原子を表す。)

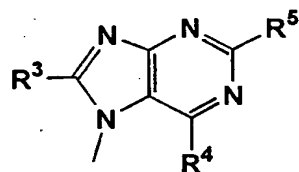
上記反応においては、最初に化合物 (XI) と化合物 (XII) とを縮合して化合物 (XIII) を調製する。N, N-ジメチルホルムアミド、テトラヒドロフラン、塩化メチレン、又は水等の適当な溶媒、あるいはこれらの溶媒を組み合わせた混合溶媒に化合物 (XI) と化合物 (XII) とを加えた後、1 等量～5 等量のトリエチルアミン、ピリジン、若しくはN, N-ジエチルアニリン等の有機塩基、又は炭酸ナトリウム、水素化ナトリウム等の無機塩基を加えて反応させ目的の化合物 (XIII) を得る。この反応は、通常、窒素あるいはアルゴン気流下、 $-20 \sim 150^\circ\text{C}$ の範囲で行なわれる。

次に、化合物 (XIII) を還元して化合物 (XIV) を得ることができる。この還元反応は、化合物 (XIII) をメタノール、エタノール、又はテトラヒドロフラン等の溶媒、あるいはこれら溶媒を組み合わせた混合溶媒に溶解させた後、10 重量%～100 重量%のラネーニッケル、パラジウムカーボン、水酸化パラジウムカーボン、又は白金などの触媒を添加し、水素気流下又は加圧下に室温～ 60°C

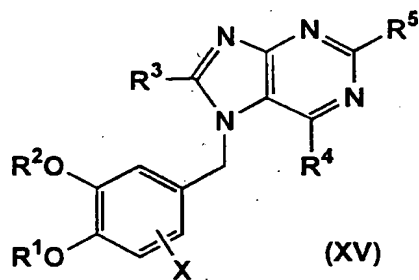
で反応させることにより行うことができる。化合物 (VII) は化合物 (XIV) を無溶媒で、あるいは1等量～5等量の酢酸、トリフルオロ酢酸、若しくはトシル酸等の有機酸又は塩酸などの無機酸の存在下で、1等量～5等量オルト蟻酸トリエチル又はオルト酢酸トリエチル等の反応剤を反応させることにより行われる。この反応は、通常、室温～250℃の範囲で行うことができる。なお、一般式 (I) の化合物の製造中間体として有用な一般式 (A) 又は一般式 (B) の化合物は、各々、上記スキーム中の一般式 (XIII) 又は (XIV) においてXが水素原子の化合物に相当する。

<製造方法3>

Aが下記の式：



で表される基である場合には、下記一般式 (XV) の化合物は、前記の一般式 (VI) 又は (IX) の化合物を用いて、製造方法1又は2と同様な方法により製造することができる。



(式中、R¹, R², R³, R⁴, R⁵、及びXは既に定義したとおりである。)

なお、N-オキシド体は、原料を一般に用いられる方法で酸化することによって製造することができる。

本発明の化合物を医薬の有効成分として用いる場合、化合物自体を投与するか、

又は薬学的に許容される製剤用添加物を用いて製造された医薬組成物として投与することができる。医薬組成物の組成は、有効成分である上記化合物の溶解度、化学的性質、投与経路、投与計画によって決定される。例えば、顆粒剤、散剤、錠剤、硬カプセル剤、軟カプセル剤、シロップ剤、乳剤、懸濁剤又は液剤等の剤形にして、経口投与してもよいし、注射剤として静脈内投与、筋肉内投与又は皮下投与してもよい。また、注射用の粉末にして用時調製して使用してもよい。

経口、経腸、非経口もしくは局所投与に適した医薬用組成物の製造には、有機又は無機の製剤用添加物を用いることができる。これらは、固体又は液体のいずれでもよく、製剤用担体又は希釈などを包含する。固形の医薬組成物を製造する際に用いられる賦形剤としては、例えば乳糖、ショ糖、デンプン、タルク、セルロース、デキストリン等が用いられる。経口投与のための液体の医薬組成物、例えば、乳剤、シロップ剤、懸濁剤、又は液剤の製造には、一般的に用いられる不活性な希釈剤、例えば水又は植物油などを用いることができる。上記の医薬組成物には、不活性な希釈剤以外に補助剤として、例えば湿潤剤、懸濁補助剤、甘味料、芳香剤、着色剤、又は保存剤などを配合することができる。液体製剤を調製してゼラチンのような体内で崩壊されうる物質のカプセル中に封入してもよい。非経口投与用の医薬組成物、例えば、注射剤等の製造に用いられる溶剤又は懸濁化剤としては、例えば水、プロピレングリコール、ポリエチレングリコール、ベンジルアルコール、オレイン酸エチル、レシチン等が挙げられる。これらの医薬組成物の製造方法は特に限定されず、当業界で利用可能な製剤の調製はすべて利用可能である。

本発明の医薬は、例えば、喘息の治療及び／又は予防のための抗喘息薬として用いることができる。本発明の医薬の投与量は、経口投与により用いる場合には、一般には成人一日あたり0.01～1000mg（有効成分重量）であり、好ましくは0.01～100mgである。もつとも、上記投与量は、患者の年齢、病状、若しくは症状、又は同時投与の医薬の有無などの種々の条件に応じて適宜増減することがさらに好ましい。また、前記の一日投与量は、1日に1回、又は適

当な間隔において1日に2から3回に分けて投与してもよく、数日ごとに間欠投与してもよい。注射剤又は点滴剤として用いる場合には、成人一日あたり0.001～100mg（有効成分重量）を連続投与又は間欠投与することが好ましい。

実施例

以下に、本発明を実施例及び試験例によりさらに具体的に説明するが、本発明の範囲は下記の実施例及び試験例に限定されるものではない。

実施例1：2-クロロ-4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-5-ニトロ-6-メチルピリミジンの合成

2, 4-ジクロロ-5-ニトロ-6-メチルピリミジン2.0gをテトラヒドロフラン14mlに溶解し、塩氷浴にて冷却（-10℃）しながら、攪拌下に3-シクロペンチルオキシ-4-メトキシベンジルアミン 2.25gをテトラヒドロフラン7mlに溶解した溶液を添加した。引き続き、トリエチルアミン1.4mlを滴下し塩氷浴（-10℃）にて30分攪拌した。反応混合物に飽和食塩水を加注した後、酢酸エチルで抽出した。有機層を無水硫酸ナトリウムで乾燥後、減圧下に濃縮し得られた残渣をエーテル・ヘキサン、50：50の混合溶媒にて懸洗し、表記の化合物3.11gを得た。

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.59-1.64 (m, 2H), 1.80-1.96 (m, 6H), 2.73 (s, 3H), 3.84 (s, 3H), 4.70 (d, 2H, $J=5.4\text{Hz}$), 4.74-4.79 (m, 1H), 6.83-6.91 (m, 3H), 8.36 (bs, 1H)

実施例2：5-アミノ-4-(3-シクロペンチルオキシ-4-メトキシベンジルアミノ)-2-クロロ-6-メチルピリミジンの合成

2-クロロ-4-(3-シクロペンチルオキシ-4-メトキシベンジル)-5-ニトロ-6-メチルピリミジン2.0gをテトラヒドロフラン14mlに溶解し、これにメタノール 14mlを加えた後、窒素雰囲気下ラネーニッケル 1.

8 gを加えた後、水素ガス雰囲気下、室温にて 4.5 時間攪拌した。反応終了後、反応懸濁液を、メタノールで洗い込みながら窒素雰囲気下セライト濾過した。得られた有機層を減圧下濃縮し、得られた残渣をエーテルから再結晶し、表記の化合物 1.65 gを得た。

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.57–1.66 (m, 2H), 1.78–1.97 (m, 6H), 2.31 (s, 3H), 2.90 (bs, 2H), 3.83 (s, 3H), 4.54 (d, 2H, $J=5.4\text{ Hz}$), 4.71–4.77 (m, 1H), 5.30 (bs, 1H), 6.79–6.93 (m, 3H)

実施例 3: 2-クロロ-9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6, 8-ジメチルプリン¹の合成 (表-2の化合物 No. 131)

5-アミノ-4-(3-シクロペンチルオキシ-4-メトキシベンジル)-2-クロロ-6-メチルピリミジン 20.0 g にオルト酢酸トリエチル 8.9 g, 酢酸 3.3 g を加え、これを 100°C で加熱し、反応途中発生するエタノールを系外に除きながら、3 時間加熱攪拌した。反応終了後、反応液を室温まで冷却した後、これに塩化メチレンを加え希釈した。この混合液を飽和重曹水で洗浄し、引き続き飽和食塩水で洗浄した後、有機層を無水硫酸マグネシウムで乾燥後、減圧下濃縮した。残渣をシリカゲルカラムクロマトグラフィー (クロロホルム: 酢酸エチル = 80:20) にて精製し、表記の化合物 18.9 g を得た。

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.59–1.63 (m, 2H), 1.76–1.90 (m, 6H), 2.58 (s, 3H), 2.80 (s, 3H), 3.81 (s, 3H), 4.64–4.68 (m, 1H), 5.28 (s, 2H), 6.70 (dd, 1H, $J=8.2, 2.0\text{ Hz}$), 6.78 (d, 1H, $J=8.2\text{ Hz}$), 6.88 (d, 1H, $J=2.0\text{ Hz}$)

実施例 4: 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6, 8-ジメチル-2-[3-(4-ピリジル)プロピルオキシ]プリン¹の合成 (表

— 2 の化合物 No. 100)

4-ピリジンプロパノール 29.91 g をテトラヒドロフラン 560 ml に溶かし、60%水素化ナトリウム 8.72 g を加え、室温で15分間攪拌した。2-クロロ-9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン 59.10 g を少量ずつ加えた後、2時間加熱還流した。冷却し、減圧下濃縮後、水を加え酢酸エチルで抽出した。有機層を飽和食塩水で洗浄し、無水硫酸マグネシウムで乾燥後、減圧下に濃縮した。残渣をシリカゲルカラムクロマトグラフィー(クロロホルム:メタノール=90:10)にて精製し、表記の化合物 68.19 g を得た。

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.54–1.81 (m, 8H), 2.15–2.22 (m, 2H), 2.86 (t, 2H, $J=6.9\text{ Hz}$), 3.80 (s, 3H), 4.43 (t, 2H, $J=6.9\text{ Hz}$), 4.62–4.64 (m, 1H), 5.23 (s, 2H), 6.67–6.79 (m, 3H), 7.16 (d, 2H, $J=6.7\text{ Hz}$), 8.48 (d, 2H, $J=6.7\text{ Hz}$)

実施例 5: 4-[[9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン]-2-イル-3-オキシプロピル]ピリジン N-オキシドの合成(表-2の化合物 No. 120)

9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[3-(4-ピリジル)プロポキシ]プリン 3 g を塩化メチレン 30 ml に溶解させた後、氷零下にて MMP (マグネシウム モノパーオキシフタレート 6 水和物) 3.85 g を蒸留水 30 ml に溶解させたものを加えた後、室温下 3 時間攪拌した。TLC にて原料の消失を確認した後、氷零下にて 5% 硫酸ナトリウム水溶液に注ぎ込み室温にて 1 時間攪拌し、過剰に存在する MMP を分解した。この反応液を塩化メチレンにて抽出した後、飽和重曹水にて洗浄し、さらに飽和食塩水にて洗浄した。得られた有機層を無水硫酸ナトリウムで乾燥しこれを減圧濃縮した。得られた残渣をシリカゲルカラムクロマトグラフィー(ク

ロロホルム：メタノール＝90：10）にて精製し、得られた化合物をTHF－ヘプタンから再結晶し、表記の化合物2.22gを得た。

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.56–1.81 (m, 8H), 2.10–2.19 (m, 2H), 2.51 (s, 3H), 2.75 (s, 3H), 2.85–2.90 (m, 2H), 3.81 (s, 3H), 4.40–4.44 (m, 2H), 4.63–4.64 (m, 1H), 5.24 (s, 2H), 6.65–6.79 (m, 3H), 7.14 (d, 2H, $J=6.7$ Hz), 8.13 (d, 2H, $J=6.7$ Hz).

実施例6： 2-クロロ-9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6-メチルアミノプリンの合成(表-2の化合物No. 136)

9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-2,6-ジクロロプリン8.07gをテトラヒドロフラン80mlに溶かし、氷浴にて冷却しながら、攪拌下にメチルアミン(40%メタノール溶液)8.0gを滴下し、室温で1時間攪拌した。減圧下濃縮後残渣に水を加え酢酸エチルで抽出した。有機層を飽和食塩水で洗浄し、無水硫酸マグネシウムで乾燥後、減圧下に濃縮し、表記の化合物7.81gを得た。

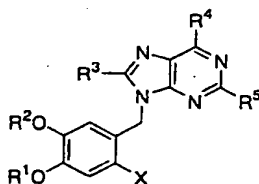
実施例7： 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6-メチルアミノ-2-(3-ピリダジニルメチルオキシ)プリンの合成(表-2の化合物No. 79)

3-ピリダジニルメタノール4.41gをN,N-ジメチルホルムアミド100mlに溶かし、60%水素化ナトリウム1.60gを加え、室温で30分間攪拌した。2-クロロ-9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6-メチルアミノプリン7.76gを少量ずつ加えた後、85℃で2時間加熱攪拌した。冷却し、減圧下濃縮後、水を加え酢酸エチルで抽出した。有機層を飽和食塩水で洗浄し、無水硫酸マグネシウムで乾燥後、減圧下濃縮した。残渣をシリカゲルカラムクロマトグラフィーにて精製し、表記の化合物3.23g

を得た。

実施例 8

実施例 1 ～ 8 の方法に準じて、下記表－ 2 及び表－ 3 記載の化合物を得た（表中、融点は℃で表す）。



表—2

化合物No	X	R1	R2	R3	R4	R5	物性
1	H	Me		H		H	無定形固体
2	H	Me		H		H	油状物
3	H	Me		H		H	mp 138-140
4	Br	Me	Me	H		H	mp 185-186
5	H	Me		H		H	mp 76-83
6	Br	Me	Me	H		H	mp 80-82
7	H	Me	Me	H		H	油状物
8	H	Me	<i>i</i> -Pr	H		H	油状物
9	H	Me		H		H	mp 142-144
10	H	Me		H		H	油状物
11	Br	Me	Me	H		H	mp 152-154
12	H	Me		H		H	mp 219-223

表—2 (つづき)


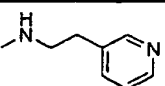

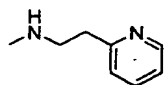

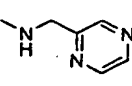

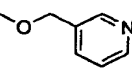

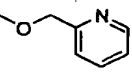

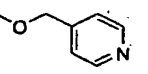

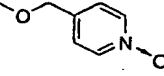

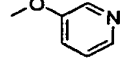

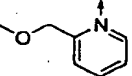
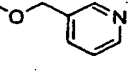

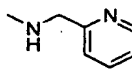

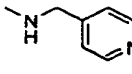

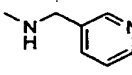

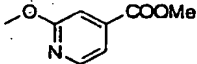
化合物No	X	R1	R2	R3	R4	R5	物性
13	H	Me		H		H	mp 113-116
14	H	Me		H		H	油状物
15	H	Me		H		H	油状物
16	H	Me		H	H		mp 114-115
17	H	Me		H	H		mp 129-130
18	H	Me		H	H		mp 105
19	H	Me		H	H		mp 105-106
20	H	Me		H	H		無定形固体
21	H	Me		H	H		mp 132
22	H	Me	<i>i</i> -Pr	H	H		mp 85-88
23	H	Me		H	H		mp 122-123
24	H	Me		H	H		mp 157-158
25	H	Me		H	H		mp 123-124
26	H	Me		H	H		mp 130-131

表-2 (つづき)


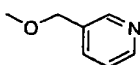

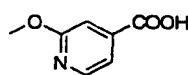

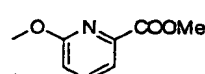

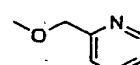

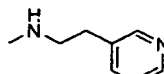

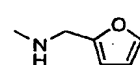

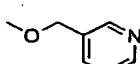

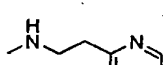

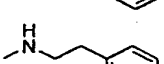

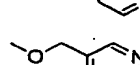

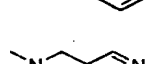

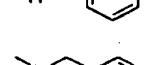

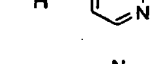

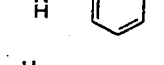
化合物No	X	R1	R2	R3	R4	R5	物性
27	H	Me		H	H		mp 114-118
28	H	Me		H	H		無定形固体
29	H	Me		H	H		mp 122-123
30	H	Me		OH	H		mp 167-169
31	H	Me		H	H		mp 110
32	H	Me		H	H		mp 159
33	H	Me		OH	H		mp 91-93
34	H	Me		H	H		mp 116-117
35	H	Me		H	H		mp 108-109
36	H	Me		Me	H		油状物
37	H	Me		Me	H		油状物
38	H	Me		Me	H		mp 181-183
39	H	Me		Me	H		mp 77-79
40	H	Me		Me	H		mp 110-112

表-2 (つづき)


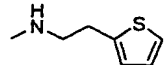

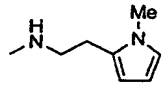

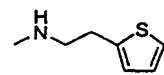

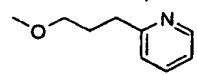

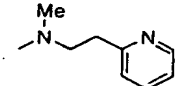

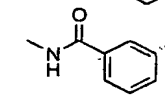

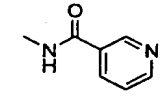

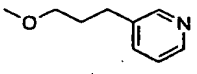

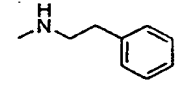

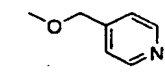

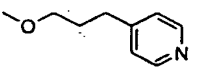

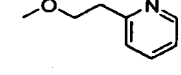

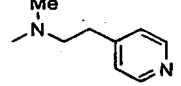

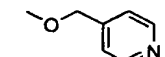
化合物No	X	R1	R2	R3	R4	R5	物性
41	H	Me		H	H		mp 141-142
42	H	Me		H	H		mp 120-121
43	H	Me		H	H		mp 112-113
44	H	Me		H	H		油状物
45	H	Me		H	H		油状物
46	H	Me		H	H		無定形固体
47	H	Me		H	H		mp 255(dec.)
48	H	Me		H	H		mp 77-78
49	H	Me		H	H		mp 110-111
50	H	Me		Me	H		mp 114-116
51	H	Me		H	H		mp 97-98
52	H	Me		H	H		油状物
53	H	Me		H	H		油状物
54	H	Me		H	H		mp 116-118

表-2 (つづき)


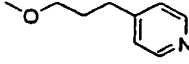

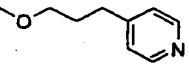
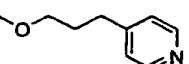
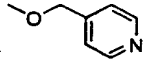

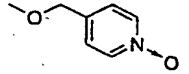

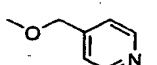

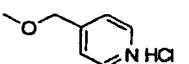

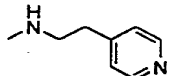

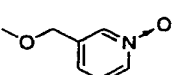

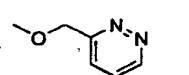

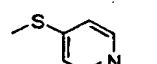

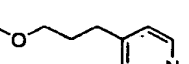

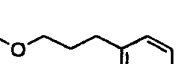

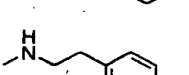
化合物No	X	R1	R2	R3	R4	R5	物性
55	H	Me		H	H		mp 128-130
56	H	Me		Me	H		mp 115-117
57	H	Me	<i>i</i> -Pr	Me	H		mp 129-132
58	H	Me	<i>i</i> -Pr	Me	H		mp 142-144
59	H	Me		Me	H		mp 183-185
60	H	Me		MeO	MeO		無定形固体
61	H	Me		Me	H		mp 154-156
62	H	Me		Me	H		無定形固体
63	H	Me		H	H		mp 161-162
64	H	Me		Me	H		mp 82-84
65	H	Me		H	H		mp 216-217
66	H	Me		H	NH ₂		mp 152-153
67	H	Me		H	Me		mp 102
68	H	Me		H	MeNH		mp 131-132

表-2 (つづき)


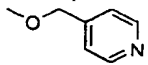

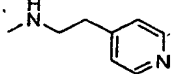

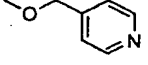

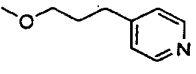

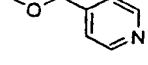

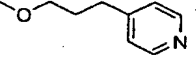

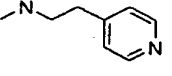

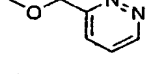

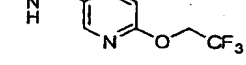

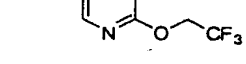

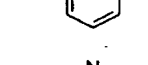

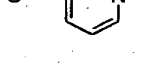

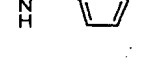


化合物No	X	R1	R2	R3	R4	R5	物性
69	H	Me		H	Me		mp 138-139
70	H	Me		H	Me		mp 105-106
71	H	Me		H	MeNH		mp 152-153
72	H	Me		H	MeNH		mp 138-140
73	H	Me		H	MeO		mp 144
74	H	Me		H	MeO		油状物
75	H	Me		H	MeO		油状物
76	H	Me		H	Me		油状物
77	H	Me		Me	H		mp 125-127
78	H	Me		Me	H		mp 99-100
79	H	Me		H	MeNH		mp 176-177
80	H	Me		H	MeO		mp 147-149
81	H	Me		H	Me		mp 141-142
82	H	Me		H	Me ₂ N		mp 78-80

表-2 (つづき)


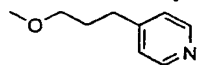

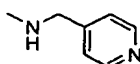

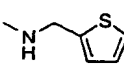


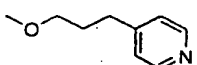

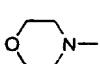
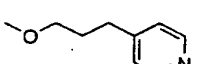

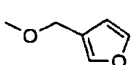

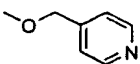

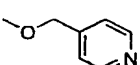
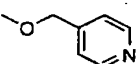

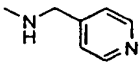

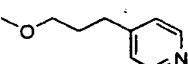
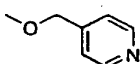

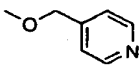

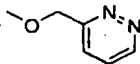
化合物No	X	R1	R2	R3	R4	R5	物性
83	H	Me		H	EtNH		mp 127-128
84	H	Me		H	Me		mp 137-138
85	H	Me		H	Me		mp 155
86	H	Me		H			mp 131-132
87	H	Me		H			mp 121
88	H	Me		H	Me ₂ N		mp 92-93
89	H	Me		H	Me ₂ N		mp 88-89
90	H	Me		Et	H		mp 134-136
91	H	Me	CF ₃ CH ₂	Me	H		mp 129-130
92	H	Me		H	Et		mp 104-106
93	H	Me		H	<i>n</i> -PrNH		mp 130-131
94	H	Me	<i>n</i> -Bu	Me	H		mp 94-97
95	H	Me		Me	Me		mp 125-126
96	H	Me		H	EtNH		mp 121-122

表-2 (つづき)

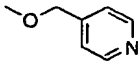

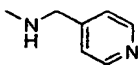

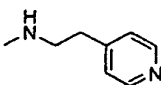

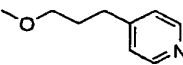

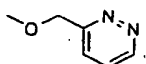

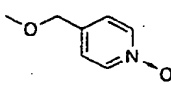

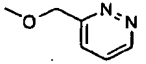

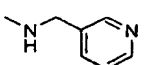

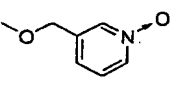
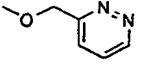
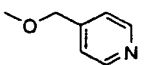

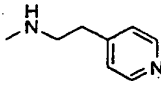

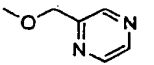

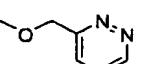
化合物No	X	R1	R2	R3	R4	R5	・物性
97	H	Me	<i>t</i> -Bu	Me	H		mp 162-163
98	H	Me		Me	Me		mp 138-139
99	H	Me		Me	Me		油状物
100	H	Me		Me	Me		mp 105-106
101	H	Me		Me	Me		無定形固体
102	H	Me		Me	Me		mp 157-158
103	H	Me		H	Me ₂ N		無定形固体
104	H	Me		H	Me ₂ N		mp 112-114
105	H	Me		Me	Me		mp 130-131
106	H	Me	<i>n</i> -Bu	H	MeNH		mp 165-166
107	H	Me	<i>n</i> -Bu	H	Me ₂ N		mp 105-107
108	H	Me		H	Et		mp 127-129
109	H	Me		Me	Me		油状物
110	H	Me		H	NH ₂		mp 141-142

表-2 (つづき)


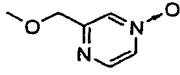

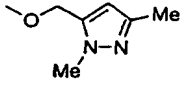

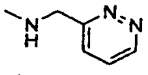

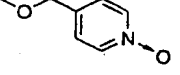

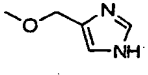

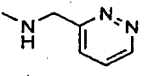

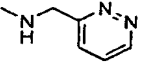

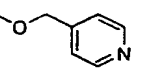

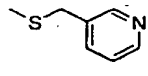

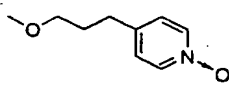

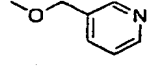

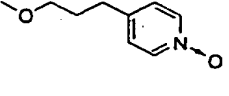

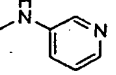

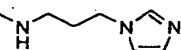

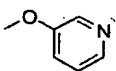







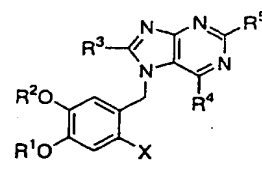

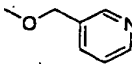

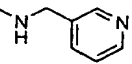

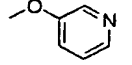
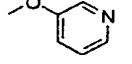
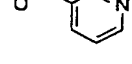
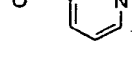
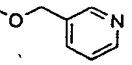


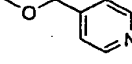
化合物No	X	R1	R2	R3	R4	R5	物性
111	H	Me		Me	Me		mp 139-140
112	H	Me		Me	Me		mp 112-123
113	H	Me		Me	Me		mp 164-166
114	H	Me		H	Me		mp 142-143
115	H	Me		Me	Me		無定形固体
116	H	Me		H	MeNH		mp 149-152
117	H	Me		H	Me		mp 161-163
118	H	Me		H	EtNH		mp 129-130
119	H	Me		Me	Me		mp 116-117
120	H	Me		Me	Me		mp 135-138
121	H	Me		Me	Me		mp 94-95
122	H	Me		H	EtNH		mp 85-88
123	H	Me		H		H	mp 181-183
124	H	Me		H	H		mp 60-61

表-2 (つづき)

化合物No	X	R1	R2	R3	R4	R5	物性
125	H	Me		Cl		Cl	mp 146-149
126	MeO	Me	Me	H	H	H	mp 119-120
127	Br	Me	Me	H	H	H	mp 161-163
128	Br	Me	Me	H	Cl	H	mp 172-173
129	Br	Me		H	H	H	mp 122-124
130	NO ₂	Me	Me	H	H	H	mp 184-186
131	H	Me		Me	Me	Cl	mp 120-122
132	H	Me		Me	Me	MeO	油状物
133	H	Me		H	Cl	Cl	mp 133-134
134	H	Me		H	NHEt	Cl	mp 129-131
135	H	Me		H	Me	Cl	mp 131-132
136	H	Me		H	NHMe	Cl	mp 155-156

表—3

							
化合物No	X	R1	R2	R3	R4	R5	物性
137	H	Me		H		H	mp 143-145
138	H	Me		H		H	mp 149-150
139	H	Me		H		H	mp 134-135
140	Br	Me	Me	H		H	mp 172-176
141	H	Me	Me	H		H	mp 137-138
142	H	Me	<i>i</i> -Pr	H		H	mp 138-142
143	Br	Me	Me	H	Cl	H	mp 171-174
144	NO ₂	Me	Me	H	H	H	mp 162-164
145	Br	Me	Me	H		H	mp 159-161
146	Br	Me		H	H	H	mp 167-169
147	H	Me		Me	H		mp 185-187
148	Br	Me	Me	H	H	H	無定形固体

下記化合物（表-2、表-3の化合物No. で表す）については、以下にNMRスペクトルを表す。

No. 1

^1H -NMR (CDCl_3) δ ppm: 1.51–1.69 (m, 2H), 1.71–1.98 (m, 6H), 3.84 (s, 3H), 4.65–4.75 (m, 1H), 5.37 (s, 2H), 6.79–6.94 (m, 3H), 7.42 (dd, 1H), 7.64–7.72 (m, 1H), 8.02 (s, 1H), 8.53–8.58 (m, 1H), 8.54 (s, 1H), 8.65 (d, 1H)

No. 2

^1H -NMR (CDCl_3) δ ppm: 1.50–1.69 (m, 2H), 1.70–1.95 (m, 6H), 3.82 (s, 3H), 4.65–4.73 (m, 1H), 5.32 (s, 2H), 5.70 (s, 2H), 6.78–6.88 (m, 3H), 7.30 (dd, 1H), 7.88 (s, 1H), 7.87–7.94 (m, 1H), 8.55–8.60 (m, 1H), 8.58 (s, 1H), 8.80 (d, 1H)

No. 7

^1H -NMR (CDCl_3) δ ppm: 3.83 (s, 3H), 3.87 (s, 3H), 5.35 (s, 2H), 5.70 (s, 2H), 6.80–6.90 (m, 3H), 7.30 (dd, 1H), 7.89 (s, 1H), 7.87–7.94 (m, 1H), 8.55–8.60 (m, 1H), 8.59 (s, 1H), 8.80 (d, 1H)

No. 8

^1H -NMR (CDCl_3) δ ppm: 1.32 (d, 6H), 3.83 (s, 3H), 4.47 (m, 1H), 5.32 (s, 2H), 5.70 (s, 2H), 6.

8.0-6.90 (m, 3H), 7.30 (dd, 1H), 7.89 (s, 1H),
7.87-7.94 (m, 1H), 8.55-8.60 (m, 1H), 8.58 (s,
1H), 8.80 (d, 1H)

No. 10

^1H -NMR (CDCl_3) δ ppm: 1.5-1.7 (m, 2H), 1.70
-1.95 (m, 6H), 3.50 (br, 3H), 3.82 (s, 3H), 4.
65-4.75 (m, 1H), 5.28 (s, 2H), 5.40 (br, 2H),
6.75-6.95 (m, 3H), 7.20-7.30 (m, 1H), 7.60
-7.70 (m, 1H), 7.70 (s, 1H), 8.43 (s, 1H), 8.
51 (m, 1H), 8.59 (s, 1H)

No. 14

^1H -NMR (CDCl_3) δ ppm: 1.59 (m, 2H), 1.81-1.
93 (m, 6H), 3.02 (t, 2H), 3.83 (s, 3H), 3.97 (m,
2H), 4.68-4.71 (m, 1H), 5.27 (s, 2H), 5.84 (m,
1H), 6.80-6.90 (m, 3H), 7.20 (d, 2H), 7.68 (s,
1H), 8.45 (s, 1H), 8.52 (d, 2H)

No. 15

^1H -NMR (CDCl_3) δ ppm: 1.50-1.70 (m, 2H), 1.
70-1.95 (m, 6H), 3.83 (s, 3H), 4.65-4.73 (m,
H), 5.34 (s, 2H), 5.84 (s, 2H), 6.80-6.95 (m,
3H), 7.91 (s, 1H), 8.50-8.60 (m, 3H), 8.85 (s,
1H)

No. 20

^1H -NMR (CDCl_3) δ ppm: 1.58–1.60(m, 2H), 1.80–1.87(m, 6H), 3.83(s, 3H), 4.65–4.75(m, 1H), 5.22(s, 2H), 6.83–6.84(m, 3H), 7.39(dd, 1H), 7.60(ddd, 1H), 7.94(s, 1H), 8.52(dd, 1H), 8.62(d, 1H), 8.89(s, 1H)

No. 28

^1H -NMR ($\text{DMSO}-d_6$) δ ppm: 1.51–1.77(m, 8H), 3.70(s, 3H), 4.44(s, 2H), 4.68(m, 1H), 6.50(d, 1H), 6.86–6.93(m, 4H), 7.84(s, 1H), 8.33(s, 2H)

No. 36

^1H -NMR (CDCl_3) δ ppm: 1.53–1.61(m, 2H), 1.70–1.81(m, 6H), 2.52(s, 3H), 3.81(s, 3H), 4.61–4.65(m, 1H), 5.27(s, 2H), 5.52(s, 2H), 6.66–6.84(m, 3H), 7.27–7.32(m, 1H), 7.84–7.88(m, 1H), 8.53–8.60(m, 1H), 8.74–8.77(m, 2H)

No. 37

^1H -NMR (CDCl_3) δ ppm: 1.53–1.59(m, 2H), 1.75–1.90(m, 6H), 2.46(s, 3H), 3.81(s, 3H), 4.59–4.63(m, 1H), 4.68(d, 2H, $J=6.0\text{ Hz}$), 5.15(m, 2H), 6.15–6.25(m, 1H), 6.62–6.78(m, 3H), 7.19(dd, 1H, $J=4.6, 7.8\text{ Hz}$), 7.70(ddd, 1H, $J=1.9, 1.9, 7.8\text{ Hz}$), 8.45(dd, 1H, $J=1.9, 4.6\text{ Hz}$), 8.53(s, 1H), 8.63(d, 1H, $J=1.9\text{ Hz}$)

No. 44

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.56–1.59 (m, 2H), 1.80–1.84 (m, 6H), 2.30–2.35 (m, 2H), 3.04 (t, 2H), 3.82 (s, 3H), 4.52 (t, 2H), 4.68–4.70 (m, 1H), 5.26 (s, 2H), 6.81–6.88 (m, 3H), 7.10–7.13 (m, 1H), 7.20 (d, 1H), 7.58 (m, 1H), 7.86 (s, 1H), 8.54 (dd, 1H), 8.86 (s, 1H)

No. 45

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.54–1.56 (m, 2H), 1.80–1.81 (m, 6H), 3.15 (t, 2H), 3.17 (s, 3H), 3.81 (s, 3H), 4.08 (t, 2H), 4.68 (m, 1H), 5.17 (s, 2H), 6.79–6.89 (m, 3H), 7.10–7.16 (m, 2H), 7.55 (m, 1H), 7.67 (s, 1H), 8.55 (d, 1H), 8.73 (s, 1H)

No. 46

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.48–1.65 (m, 2H), 6.93 (dd, 1H), 8.99 (s, 1H), 1.68–1.98 (m, 6H), 7.00 (d, 1H), 3.83 (s, 3H), 4.70–4.80 (m, 1H), 5.34 (s, 2H), 6.84 (d, 1H), 7.48–7.64 (m, 3H), 7.94 (s, 1H), 7.94–8.01 (m, 2H), 8.79 (br s, 1H)

No. 52

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.55–1.58 (m, 2H), 1.76–1.83 (m, 6H), 3.36 (t, 2H), 3.82 (s, 3H), 4.68–4.70 (m, 1H), 4.85 (t, 2H), 5.25 (s, 2H), 6.80–

6. 87 (m, 3H), 7. 12-7. 16 (m, 1H), 7. 31 (d, 1H), 7. 62 (ddd, 1H), 7. 84 (s, 1H), 8. 56 (d, 1H), 8. 86 (s, 1H)

No. 53

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1. 56 (m, 2H), 1. 81 (m, 6H), 2. 95 (t, 2H), 3. 18 (s, 3H), 3. 81 (s, 3H), 3. 94 (t, 2H), 4. 68 (m, 1H), 5. 18 (s, 2H), 6. 80-6. 87 (m, 3H), 7. 16 (d, 2H), 7. 67 (s, 1H), 8. 49 (d, 2H), 8. 74 (s, 1H)

No. 60

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1. 47-1. 67 (m, 2H), 1. 71-2. 01 (m, 6H), 3. 80 (s, 3H), 4. 09 (s, 3H), 4. 17 (s, 3H), 4. 63-4. 75 (m, 1H), 5. 03 (s, 2H), 5. 47 (s, 2H), 6. 70 (d, 1H), 6. 75 (dd, 1H), 6. 93 (d, 1H), 7. 38 (d, 2H), 8. 59 (d, 2H)

No. 62

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 2. 00-2. 15 (m, 2H), 2. 46 (s, 3H), 2. 96 (t, 2H), 3. 70-4. 03 (m, 6H), 3. 82 (s, 3H), 4. 78-4. 85 (m, 1H), 5. 19 (s, 2H), 5. 20 (brs, 1H), 6. 70-6. 85 (m, 3H), 7. 17 (d, 2H), 8. 51 (d, 2H), 8. 57 (s, 1H)

No. 74

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1. 56-1. 58 (m, 2H), 1. 7

6-1. 84(m, 6H), 2. 17-2. 22(m, 2H), 2. 85(t, 2H), 3. 82(s, 3H), 4. 16(s, 3H), 4. 45(t, 2H), 4. 67-4. 68(m, 1H), 5. 20(s, 2H), 6. 81-6. 82(m, 3H), 7. 16(d, 2H), 7. 68(s, 1H), 8. 50(d, 2H)

No. 75

^1H -NMR (CDCl_3) δ ppm: 1. 56(m, 2H), 1. 81(m, 6H), 2. 96(t, 2H), 3. 74(q, 2H), 3. 81(s, 3H), 4. 07(s, 3H), 4. 66-4. 68(m, 1H), 5. 07(t, 1H), 5. 15(s, 2H), 6. 81(m, 3H), 7. 16(d, 2H), 7. 54(s, 1H), 8. 52(d, 2H)

No. 76

^1H -NMR (CDCl_3) δ ppm: 1. 59(m, 2H), 1. 80-1. 83(m, 6H), 2. 79(s, 3H), 3. 83(s, 3H), 4. 70(m, 1H), 5. 22(s, 2H), 5. 88(s, 2H), 6. 82(m, 3H), 7. 48(d, 1H), 7. 79(d, 2H), 7. 83(s, 1H), 9. 15(d, 1H)

No. 99

^1H -NMR (CDCl_3) δ ppm: 1. 50-1. 85(m, 8H), 2. 46-2. 52(m, 3H), 2. 63-2. 75(m, 3H), 2. 88-2. 97(m, 2H), 3. 54-3. 58(m, 2H), 3. 81(s, 3H), 4. 54-4. 58(m, 1H), 4. 63(b r s, 1H), 5. 16-5. 24(m, 2H), 6. 67-6. 79(m, 3H), 7. 14-7. 18(m, 2H), 8. 49-8. 52(m, 2H)

No. 101

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.50–1.60(m, 2H), 1.75–1.90(m, 6H), 2.54(s, 3H), 2.76(s, 3H), 3.81(s, 3H), 4.60–4.70(m, 1H), 5.23(s, 2H), 5.86(s, 2H), 6.64–6.78(m, 3H), 7.48(dd, 1H, $J=4.9, 8.5$ Hz), 7.79(dd, 1H, $J=1.5, 8.5$ Hz), 9.14(dd, 1H, $J=1.5, 4.9$ Hz)

No. 103

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.50–1.64(m, 2H), 5.81(s, 2H), 1.70–1.94(m, 6H), 6.70–6.90(m, 3H), 3.40(b r s, 6H), 3.82(s, 3H), 4.64–4.72(m, 1H), 5.15(s, 2H), 7.44(dd, 1H), 7.53(s, 1H), 7.72(dd, 1H), 9.11(dd, 1H)

No. 109

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.50–1.60(m, 2H), 1.70–1.90(m, 6H), 2.52(s, 3H), 2.76(s, 3H), 3.81(s, 3H), 4.60–4.70(m, 1H), 5.22(s, 2H), 5.66(s, 2H), 6.63–6.83(m, 3H), 8.52–8.55(m, 2H), 8.86(s, 1H)

No. 115

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1.50–1.60(m, 2H), 1.60–1.90(m, 6H), 2.59(s, 3H), 2.82(s, 3H), 3.81(s, 3H), 4.60–4.65(m, 2H), 4.69(s, 1H), 5.31(s, 2H), 6.72–6.82(m, 3H), 7.94(d, 1H, $J=1.2$ Hz),

8. 65 (d, 1H, $J=1.2$ Hz)

No. 120

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1. 56–1. 81 (m, 8H), 2. 10–2. 19 (m, 2H), 2. 51 (s, 3H), 2. 75 (s, 3H), 2. 85–2. 90 (m, 2H), 3. 81 (s, 3H), 4. 40–4. 44 (m, 2H), 4. 63–4. 64 (m, 1H), 5. 24 (s, 2H), 6. 65–6. 79 (m, 3H), 7. 14 (d, 2H, $J=6.7$ Hz), 8. 13 (d, 2H, $J=6.7$ Hz).

No. 132

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 1. 50–1. 90 (m, 8H), 2. 52 (s, 3H), 2. 74 (s, 3H), 3. 81 (s, 3H), 4. 05 (s, 3H), 4. 62–4. 64 (m, 1H), 5. 25 (s, 3H), 6. 70–6. 79 (m, 3H)

No. 148

$^1\text{H-NMR}$ (CDCl_3) δ ppm: 3. 80 (s, 3H), 3. 90 (s, 3H), 5. 46 (s, 2H), 6. 72 (s, 1H), 7. 10 (s, 1H), 8. 29 (s, 1H), 8. 85 (s, 1H), 9. 15 (s, 1H)

実施例9：錠剤の製造

よく粉砕した9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[3-(4-ピリジル)プロピルオキシ]プリン(表-2の化合物No. 100) 1000g、乳糖5900g、結晶セルロース2000g、低置換度ヒドロキシプロピルセルロース1000g、ステアリン酸マグネシウム100gをよく混合し、直接打錠法にて1錠100mg中前記化合物10mgを

含有する素錠を製造した。この素錠に糖衣またはフィルムコートを施して、糖衣錠およびフィルムコーティング錠を製造した。

実施例 10 : カプセル剤の製造

よく粉砕した 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6-メチルアミノ-2-[(3-ピリダジニル)メチルオキシ]プリン (表-2の化合物 No. 79) 1000 g、トウモロコシデンプン 3000 g、乳糖 6900 g、結晶セルロース 1000 g、ステアリン酸マグネシウム 100 g を混和して 1 カプセル 12.0 mg 中前記化合物 10 mg を含有するカプセル剤を製造した。

実施例 11 : 吸入剤の製造

よく粉砕した 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6-エチルアミノ-2-[(3-ピリダジニル)メチルオキシ]プリン (表-2の化合物 No. 96) 5 g、中鎖飽和脂肪酸トリグリセリド 10 g、ソルビタンモノレオート 0.2 g をよく混合し、混和物各 15.2 mg を 5 ml のエアゾール用アルミ容器に秤取し、さらに、1 容器当りフレオン 12/114 (1:1 混合物) 84.8 mg を低温充填した後、1 噴射 10.0 μ l の定量アダプターをとりつけ、1 容器 5 ml 中、前記化合物 5 mg を含有する定量噴霧の吸収剤を製造した。

試験例

本発明の化合物の PDE IV 阻害作用を検討した。対照として用いたロリプラムは特開昭 50-157360 号公報に記載された化合物であり、その構造は本明細書の従来技術の欄に示した。この化合物が PDE IV に対して特異的な阻害作用を有することは、Adv. Second Messenger Phosphoprotein Res., 22, 1 (1988) 等に記載されている。

試験例 1 : I V 型ホスホジエステラーゼ (PDE IV) の酵素活性に対する作用

酵素はヒト単球様細胞株 U 9 3 7 細胞質分画より Nicholson ら [Br. J. Pharmacol., 97, 889 (1989)] の方法に準じて Q-セファロースカラムにより粗精製し、日高ら [Biochem. Med., 10, 301 (1974)] の方法に準じて $0.4 \mu\text{M}$ ^3H -cAMP を基質として 0.1 mg/ml BSA、 1 ml EDTA、 5 mM MgCl_2 、 50 mM トリス緩衝液 (pH 8.0) 中で 30°C にて 15 分間反応させ、生じた ^3H -5'-AMP を陽イオン交換カラムで分離、放射エネルギーを測定することにより酵素活性を測定した。試験化合物を添加し、 30°C にて 15 分間インキュベーションした後、基質を添加して、試験化合物未添加時の反応を 100% とし、各濃度における阻害率を求め、プロット解析を用いて 50% 阻害率を示す濃度 (IC_{50}) を算出した。その結果を表 4 に示す。

表 4

化合物 No.	PDE	I V 阻害作用	IC_{50} (M)
2	8.9	$\times 10^{-9}$	
32	1.2	$\times 10^{-9}$	
36	2.6	$\times 10^{-9}$	
37	1.0	$\times 10^{-9}$	
39	1.4	$\times 10^{-9}$	
41	4.7	$\times 10^{-10}$	
55	4.5	$\times 10^{-9}$	
56	1.3	$\times 10^{-9}$	
57	4.6	$\times 10^{-9}$	
66	1.4	$\times 10^{-9}$	
72	7.5	$\times 10^{-10}$	
77	8.3	$\times 10^{-10}$	
78	1.3	$\times 10^{-9}$	

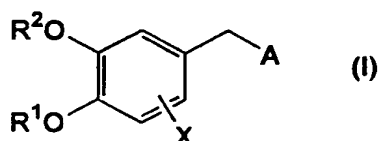
79	4.7	×	10^{-9}
81	3.5	×	10^{-10}
82	8.2	×	10^{-10}
83	6.9	×	10^{-10}
84	1.9	×	10^{-9}
85	1.3	×	10^{-10}
88	2.0	×	10^{-10}
93	4.4	×	10^{-10}
95	1.7	×	10^{-9}
96	3.8	×	10^{-9}
98	1.0	×	10^{-9}
100	5.5	×	10^{-10}
101	6.1	×	10^{-9}
102	1.5	×	10^{-8}
104	1.1	×	10^{-9}
112	2.2	×	10^{-10}
113	2.4	×	10^{-8}
119	6.4	×	10^{-10}
120	2.0	×	10^{-9}
122	1.5	×	10^{-8}
131	6.7	×	10^{-9}
134	4.1	×	10^{-8}
136	7.4	×	10^{-8}
137	6.4	×	10^{-8}
139	5.4	×	10^{-8}
ロリプラム	3.0	×	10^{-7}

産業上の利用可能性

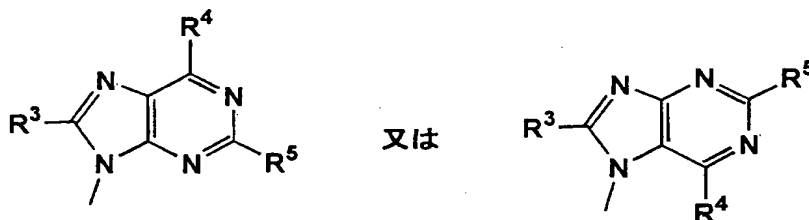
一般式 (I) で表される本発明の化合物は優れた P D E IV 阻害作用を有しており、喘息等の治療及び／又は予防のための医薬の有効成分として有用である。また、一般式 (A) 又は (B) で表される化合物は、上記の式 (I) で表される化合物の製造用中間体として有用である。

請求の範囲

1. 下記一般式 (I) :



[式中、 R^1 は $C_1 \sim C_4$ のアルキル基又はジフルオロメチル基を表し； R^2 はテトラヒドロフラン基、 $C_1 \sim C_7$ のアルキル基、 $C_1 \sim C_7$ のハロアルキル基、 $C_2 \sim C_7$ のアルケニル基、ビシクロ[2, 2, 1]ヘプト-2-イル基、又は $C_3 \sim C_8$ のシクロアルキル基を表し；Xは水素原子、ハロゲン原子、又はニトロ基を表し；Aは下記の式：



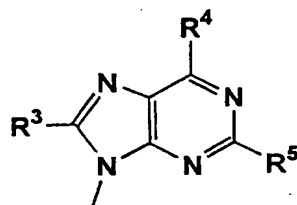
[式中、 R^3 は水素原子、ハロゲン原子、水酸基、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基を表し； R^4 及び R^5 はそれぞれ独立に水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、ピロリジニル基、モルホリノ基、 $C_2 \sim C_8$ のジアルキルアミノ基、又は $-Y-(CH_2)_n-B$ {Yは $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-N(R^6)-$ (R^6 は水素原子又は $C_1 \sim C_4$ のアルキル基を表す) を表し、 n は0~4の整数を表し、Bはそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基を表す} で示される基を表す] で示される基を表すが、

ただし、Xが水素原子を表す場合、 R^4 又は R^5 のいずれかは $-Y-(CH_2)_n-B$ {Yは $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-N(R^6)-$ (R^6 は水素原子又は $C_1 \sim C_4$ のアルキル基を表す)を表し、

(i) Yが $-O-$ 、 $-S-$ 、又は $-NHCO-$ を表す場合には、nは0～4の整数を表し、Bはそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基を表し、

(ii) Yが $-N(R^6)-$ を表す場合には、nは1～4の整数を表し、Bは複素環残基を表す]で示される基を表す]で表されるプリン誘導体、その塩、若しくはそのN-オキシド体、又はそれらの水和物若しくはそれらの溶媒和物。

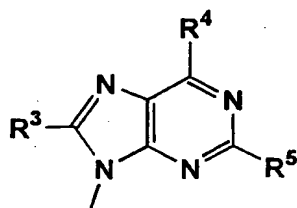
2. Aが下記の式：



[R^3 は水素原子、ハロゲン原子、水酸基、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基であり； R^4 及び R^5 の一方が水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、ピロリジニル基、モルホリノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基であり、他方が $-Y-(CH_2)_n-B$ (Yは $-O-$ 、 $-S-$ 、 $-NHCO-$ 、又は $-N(R^6)-$ (R^6 は水素原子又は $C_1 \sim C_4$ のアルキル基を表す)であり、nが0～4の整数であり、Bがそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基である]で示される基である請求の範囲第1項に記載のプリン誘導体、その塩、若しくはそのN-オキシド体、又はそれらの水和物若しくはそれらの溶媒和物。

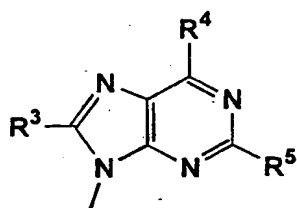
3. R^1 が $C_1 \sim C_4$ のアルキル基であり、 R^2 がテトラヒドロフラニル基、 $C_1 \sim$

C₆のアルキル基、C₁～C₃のハロアルキル基、又はC₃～C₈のシクロアルキル基であり、Aが下記の式：



{R³が水素原子、ハロゲン原子、水酸基、C₁～C₄のアルキル基、又はC₁～C₄のアルコキシ基であり；R⁴が水素原子、ハロゲン原子、C₁～C₄のアルキル基、C₁～C₄のアルコキシ基、C₁～C₄のアルキルアミノ基、又はC₂～C₈のジアルキルアミノ基であり、R⁵が-Y-(CH₂)_n-B（Yは-O-、-S-、又は-NHCO-であり、nが1～4の整数であり、Bが置換基を有していてもよい複素環残基である）で表される基である} で表される基である請求の範囲第1項に記載のプリン誘導体、その塩、若しくはそのN-オキシド体、又はこれらの水和物若しくはこれらの溶媒和物。

4. R¹がC₁～C₃のアルキル基であり、R²がC₃～C₈のシクロアルキル基であり、Aが下記の式：



{R³が水素原子、C₁～C₃のアルキル基、又はC₁～C₃のアルコキシ基であり；R⁴はC₁～C₃のアルキル基、C₁～C₃のアルコキシ基、C₁～C₃のアルキルアミノ基であり；R⁵が-Y-(CH₂)_n-B（Yが-O-であり、nは1～4の整数であり、Bが置換基を有していてもよい複素環残基である）で表される基

である} で表される基である請求の範囲第1項に記載のプリン誘導体、その塩、若しくはそのN-オキシド体、又はそれらの水和物若しくはそれらの溶媒和物。

5. 2-クロロ-9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

6. 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-メトキシプリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

7. 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-(3-ピリダジニルメチルオキシ)プリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

8. 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[4-ピリジルメチルオキシ]プリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

9. 4-[[9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン]-2-イル-オキシメチル]ピリジン N-オキシド若しくはその塩、又はそれらの水和物若しくは溶媒和物。

10. 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[2-(4-ピリジル)エチルオキシ]プリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

11. 4-[[9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン]-2-イル-2-オキシエチル]ピリジン N-オキシド若しくはその塩、又はそれらの水和物若しくは溶媒和物。

12. 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6-メチルアミノ-2-(3-ピリダニルメチルオキシ)プリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

13. 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-

ジメチル-2-[2-(4-ピリジル)エチルアミノ]プリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

14. 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[(4-ピリジル)メチルアミノ]プリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

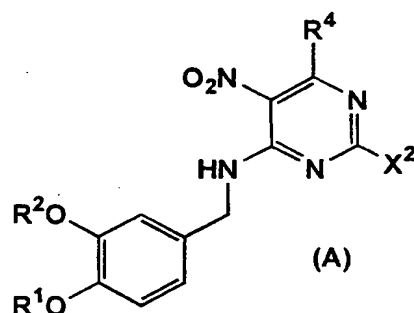
15. 9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチル-2-[3-(4-ピリジル)プロピルオキシ]プリン若しくはその塩、又はそれらの水和物若しくは溶媒和物。

16. 4-[[9-[(3-シクロペンチルオキシ-4-メトキシ)ベンジル]-6,8-ジメチルプリン]-2-イル-3-オキシプロピル]ピリジン N-オキシド若しくはその塩、又はそれらの水和物若しくは溶媒和物。

17. 請求の範囲第1項ないし第16項のいずれか1項に記載のプリン誘導体、その塩、及びそのN-オキシド体、並びにそれらの水和物及びそれらの溶媒和物からなる群から選ばれる物質を有効成分として含む医薬。

18. 抗喘息薬である請求の範囲第17項に記載の医薬。

19. 下記の一般式(A)：

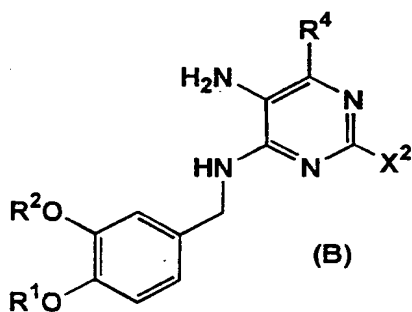


〔式中、 R^1 は $C_1 \sim C_4$ のアルキル基又はジフルオロメチル基を表し； R^2 はテトラヒドロフラニル基、 $C_1 \sim C_7$ のアルキル基、 $C_1 \sim C_7$ のハロアルキル基、 $C_2 \sim C_7$ のアルケニル基、ビスクロ[2, 2, 1]ヘプト-2-イル基、又は $C_3 \sim C_8$ のシクロアルキル基を表し； R^4 は水素原子、ハロゲン原子、 $C_1 \sim C_4$ の

アルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、ピロリジニル基、モルホリノ基、 $C_2 \sim C_8$ のジアルキルアミノ基、又は— $Y-(CH_2)_n-B$ { Y は— O —、— S —、— $NHCO$ —、又は— NR^6 — (R^6 は水素原子又は $C_1 \sim C_4$ のアルキル基を表す)を表し、 n は0～4の整数を表し、 B はそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基を表す}を表し、 X^2 はハロゲン原子を表す]で示される化合物。

20. R^1 が $C_1 \sim C_4$ のアルキル基であり、 R^2 がテトラヒドロフラニル基、 $C_1 \sim C_6$ のアルキル基、 $C_1 \sim C_3$ のハロアルキル基、 $C_3 \sim C_8$ のシクロアルキル基であり、 R^4 は水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基である請求の範囲第19項に記載の化合物。

21. 下記の一般式 (B) :



[式中、 R^1 は $C_1 \sim C_4$ のアルキル基又はジフルオロメチル基を表し； R^2 はテトラヒドロフラニル基、 $C_1 \sim C_7$ のアルキル基、 $C_1 \sim C_7$ のハロアルキル基、 $C_2 \sim C_7$ のアルケニル基、ビスクロ[2, 2, 1]ヘプト-2-イル基、又は $C_3 \sim C_8$ のシクロアルキル基を表し； R^4 は水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、アミノ基、 $C_1 \sim C_4$ のアルキルアミノ基、ピロリジニル基、モルホリノ基、 $C_2 \sim C_8$ のジアルキルアミノ基、又は— $Y-(CH_2)_n-B$ { Y は— O —、— S —、— $NHCO$ —、又は— $N(R^6)$ — (R^6 は水素原子又は $C_1 \sim C_4$ のアルキル基を表す)を表し、 n は0～4の整

数を表し、Bはそれぞれが置換基を有していてもよいフェニル基、ナフチル基、又は複素環残基を表す}を表し、 X^2 はハロゲン原子を表す]で示される化合物。

22. R^1 が $C_1 \sim C_4$ のアルキル基であり、 R^2 がテトラヒドロフラニル基、 $C_1 \sim C_6$ のアルキル基、 $C_1 \sim C_3$ のハロアルキル基、 $C_3 \sim C_8$ のシクロアルキル基であり、 R^4 は水素原子、ハロゲン原子、 $C_1 \sim C_4$ のアルキル基、 $C_1 \sim C_4$ のアルコキシ基、 $C_1 \sim C_4$ のアルキルアミノ基、又は $C_2 \sim C_8$ のジアルキルアミノ基である請求の範囲第21項に記載の化合物。

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP98/05092

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl.⁶ C07D473/00, C07D473/06, C07D473/16, C07D473/18, C07D473/28, C07D473/32, C07D473/34, 361, C07D473/40, C07D239/48, C07D239/50,

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl.⁶ C07D473/00-473/40, C07D239/48, C07D239/50, A61K31/52, A61K31/535

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Caplus (STN), REGISTRY (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, 3862189, A (Warner-Lambert Company), 21 Jan. 1975 (21. 01. 75) (Family: none)	1-17, 19-22
A	US, 3936454, A (Warner-Lambert Company), 3 Feb. 1976 (03. 02. 76) (Family: none)	1-17, 19-22
A	JP, 8-231545, A (Bayer AG.), 10 September, 1996 (10. 09. 96) & EP, 722944, A1 & DE, 19501482, A1 & FI, 9600225, A & CA, 2167353, A & CN, 1135485, A	1-22

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search
1 February, 1999 (01. 02. 99)

Date of mailing of the international search report
9 February, 1999 (09. 02. 99)

Name and mailing address of the ISA/
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP98/05092

A. (Continuation) CLASSIFICATION OF SUBJECT MATTER

A61K31/52, A61K31/535

国際調査報告

国際出願番号 PCT/J P 98/05092

A. 発明の属する分野の分類 (国際特許分類 (IPC))

Int. Cl.⁸ C07D473/00, C07D473/06, C07D473/16, C07D473/18, C07D473/28, C07D473/32, C07D473/34 361, C07D473/40, C07D239/48, C07D239/50, A61K31/52, A61K31/535

B. 調査を行った分野

調査を行った最小限資料 (国際特許分類 (IPC))

Int. Cl.⁸ C07D473/00-473/40, C07D239/48, C07D239/50, A61K31/52, A61K31/535

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)

CAplus (STN), REGISTRY (STN)

C. 関連すると認められる文献

引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
A	US, 3862189, A (Warner-Lambert Company) 21. Jan. 1975 (21. 1. 75) (ファミリーなし)	1-17, 19-22
A	US, 3936454, A (Warner-Lambert Company) 3. Feb. 1976 (03. 02. 76) (ファミリーなし)	1-17, 19-22
A	JP, 8-231545, A (バイエル・アクチエンゲゼルシャフト) 10. 9月. 1996 (10. 09. 96) &EP, 722944, A1 &DE, 19501482, A1 &FI, 9600225, A &CA, 2167353, A &CN, 1135485, A	1-22

☐ C欄の続きにも文献が列挙されている。☐ パテントファミリーに関する別紙を参照。

* 引用文献のカテゴリー

「A」 特に関連のある文献ではなく、一般的技術水準を示すもの

「E」 国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの

「L」 優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献 (理由を付す)

「O」 口頭による開示、使用、展示等に言及する文献

「P」 国際出願日前で、かつ優先権の主張の基礎となる出願

の日の後に公表された文献

「T」 国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの

「X」 特に関連のある文献であって、当該文献のみで発明の新規性又は進歩性がないと考えられるもの

「Y」 特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの

「&」 同一パテントファミリー文献

国際調査を完了した日

01. 02. 99

国際調査報告の発送日

09.02.99

国際調査機関の名称及びあて先

日本国特許庁 (ISA/J P)

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